PNEUMOCONIOSIS

Industrial Diseases of the Lung caused by Dust

By

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PREFACE

Fifty years ago pneumoconiosis was a word which belonged exclusively to the vocabulary of the medical practitioner and it was seldom used even by him Now pneumoconiosis is recognised as the most serious industrial disease Legislation has been introduced to regulate the conditions in factories where operations give rise to dust and to provide for the compensation of sufferers In some industries agreement has been reached on maximum permissible dust levels and these are enforced by law Special ventilation methods have been designed to reduce the dust levels in industrial atmospheres, and in some works the periodic check on dust levels is an established routine, as is the regular medical examination of all personnel

Quite apart from the research workers who are studying the disease and the dusts which cause it, an increasing number of scientists, medical specialists, physicists, chemists, engineers, and administrators have become involved in the pneumoconiosis problem The papers in which the various aspects of the disease are discussed are widely scattered in many types of journals and it is often difficult for a worker to find information on matters outside his own field The intention of this book is to provide sufficient material to act as an introduction and to indicate where further information can be found Each chapter reviews one aspect of the subject with enough detail to give a true picture of the present position, but no lengthy discussion, which properly belongs to a more specialised book, has been attempted

Throughout this book an attempt has been made to emphasise the controversial nature of much of the information This, it is hoped, may counteract the reliance which is sometimes shown on one or other of the many theories which have been advanced Undoubtedly, less stringent precautions against dust are sometimes taken because on theoretical grounds, a particular dust is presumed to have a low pathogenicity It cannot be emphasised too strongly that any dust must be regarded as a health hazard unless specific investigations have proved it otherwise, and this statement applies particularly to silica dust in all its forms If this book facilitates the work of anyone interested in the problem of pneumoconiosis, it has served its purpose

'Pneumoconiosis' is the name given to a group of lung diseases caused by inhalation of dust.

CHAPTER 1

INTRODUCTION

For centuries it has been known that certain lung diseases are associated with dusty occupations. In 1866 Zenker[1] used the word "pneumonokoniosis" to describe these diseases and this word was abbreviated by Proust[2] in 1874 to "pneumoconiosis". In the National Insurance (Industrial Injuries) Act, 1946, Section 57 (3), pneumoconiosis is defined as 'fibrosis of the lungs due to silica dust, asbestos dust or other dust and includes the condition of the lungs known as dust reticulation but does not include byssinosis". Byssinosis is a condition of the lung which results from the inhalation of cotton dust.

It is impossible to say how widespread was the incidence of pneumoconiosis until very recent times. The symptoms of pneumoconiosis and those of tuberculosis are very similar. 'It must be accepted as a fact that dust induces a malady bearing a strong similitude to tubercular phthisis, and yet that the malady is not tubercular in its actual nature" (Aldridge[3] 1892). Before the discovery of the tubercle bacillus in 1882, conditions of the lung produced by dust could not be differentiated with certainty from tuberculosis, indeed differentiation between pneumoconiosis and other pathological conditions of the lung was seldom made until some fifty years later. Even in 1919 Landis[4] introduced a paper on dust diseases by the statement 'Pneumoconiosis occupies a curious position. The term is a familiar one and the nature of the disorder is described in all textbooks dealing with diseases of the lungs. In spite of this the term is rarely used by the clinician and only a little less frequently by the pathologist. One may search statistics dealing with morbidity and mortality rates and find no mention of the condition. In those instances in which the deposition of dust in the respiratory system has actually given rise to pathological changes, the illness or the cause of death is ascribed to secondary changes, such as chronic bronchitis, asthma or tuberculosis. The etiological factor is thus concealed by the use of other terms". For a long time the inhalation of any dust was considered to predispose to tuberculosis, a disease widely prevalent amongst factory operatives in the

eighteenth and nineteenth centuries Not until 1913 did Collis[5] point out that the nature of the respiratory disease caused by dust

inhalation of flax dust, particularly as it affected child workers. "Children from 7 to 15 years of age go to work at half past five in the morning and leave at seven in the evening and thus spend twelve hours a day, for five or six years, in an atmosphere of flax dust."

this entering the channel will draw down the greater part of the dust, and carry it out of the building." However, Beddoes[7] in 1799 attributed the high mortality from phthisis in the textile industry to confinement and inactivity rather than to dust.

Silicosis and asbestosis must be the oldest of industrial diseases since materials known to cause these diseases are amongst those used by earliest man The manufacture of gunflints at Brandon, Sussex, and at Meusnes in France was associated with a terrible mortality among the workers, who used implements little different from the deerhorn picks with which flints were shaped in the palaeolithic period, so it seems likely that silicosis existed in prehistoric times.[8] Although the pyramids were built from limestone, the dust of which is harmless, the Egyptians (3000-2000 B.C.) used granite for their doors and for building altars and obelisks.[9] The Egyptians also mined gold which was found in quartz veins. The quartz was crushed in mortars and ground to a powder, then the gold was separated by levigation Signs of pneumoconiosis were found in a number of Egyptian mummies.[10] The fact that the

stant dust enters the blood and lungs, producing the difficulty of breathing which the Greeks call asthma. When the dust is corrosive it ulcerates the lungs and produces consumption; hence it is that in the Carpathian Mountains there are women who have married

seven husbands, all of whom this dreadful disease has brought to an early grave."

Agricola advocated the ventilation of mines not only because of the effects of noxious gases and dust on the miners but also because their lights would not burn. "These lights, too, burn feebly, whilst they give out a worse emanation than men do." Brard[18] (1788) mentioned that glow-worms were used for illumination when a light would not burn. The conditions in the mines at this time were very bad and it is not surprising that in *Bericht von Bergwercken* of 1690, there were published oaths for each class of the mining community, and prayers for all their conditions!



Fig. 1.1. Stamp Mill for crushing flints for the manufacture of Porcelain (Tomlinson, *Illustrations of Useful Arts, Manufactures and Trades* 1867)

As industries developed and siliceous materials were used in increasing quantities pneumoconiosis became more common. The industries involved can be judged by the names under which the disease was known in different parts of the country: mason's disease, potters' rot, grinders' asthma, miners' disease, miners' asthma and sewer disease.

During the eighteenth century a high phthisis mortality was noted

amongst workers manufacturing millstones, stone-cutters and

Arts, Manufactures and Trades (1867): "The third process is pointing or grinding the ends of the wires on a grit stone. Several thousand wires can be pointed at both ends in an hour. A stream of sparks accompanies the contact of the wires and the stone, and minute particles of grit and steel fill the air of the room, and, entering the workman's lungs, produce a disease called the 'grinders' asthma'."

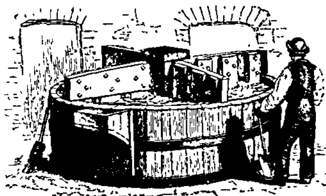


Fig 1 2 Flint Pan used in the wet grinding of flint (Tomlinson *Illustrations of Useful Arts, Manufactures and Trades*, 1867)

Josiah Wedgwood introduced finely powdered calcined flint into his white pottery in 1720. The high concentration of air-borne silica dust which resulted when the dry flints were ground and sieved produced lung diseases in the operatives. A wet grinding process was later adopted.[15] Machines used in the crushing of calcined flints and the wet grinding of the crushed flints are shown in Figs 1.1 and 1 2.

With the introduction of steam power in the nineteenth century there was a notable increase in silicosis, particularly in trades such as knife grinding From the record of 61 persons engaged in this trade who died between 1825 and 1840, Holland[16] found that 35 died before the age of 30.

The effects of the lethal granite dust in the Cornish copper- and tin mines in the middle of the nineteenth century is evident from statistics given in Tables 1 1 and 1 2 quoted in the report of the

TABLE 1 1

Extract from the Report of the Chief of the Statistical Department in the General Register Office 1863

Out of 10 000 males who attain the age of 15 there were registered as dying from consumption and other lung diseases

Age group	In England	Of Cornish miners	Difference
15	351	292	59 less
25	417	387	30
35	417	660	243 more
45	454	1 498	1 044
55	500	1 709	1 209
65 to 75	469	930	461
Total	2 608	5 476	2 868 more

TALLF 1 2

Extracts from the Report of the Chief of the Statistical Department in the General Register Office 1863

Out of 10 000 males who attain the age of 15 there were registered as dying of the following diseases

	In England all occupations	Miners in			
		Cornwall	Stafford	Durham	S Wales
Diarrhoea and cholera	547	230	1 052	1 255	1 915
Fever	426	324	385	307	782
Diseased heart and dropsy	928	484	612	928	333
Consumption	1 523	4 439	660	948	1 604
Other lung disease	1 343	1 157	1 975	1 010	1 433
Accident or violence	532	782	2 782	1 312	2 158
All lung disease	2 866	5 596	2 655	1 958	3 037
Lung disease and accident	3 498	6 378	5 437	3 270	5 195

Royal Commissioners appointed in 1862 to inquire into the health of workers in metalliferous mines The figures, which refer to the yea

in

far

smaller particles of granite and other hard and gritty earthy matters which are thrown off from the rock by their tools, such must certainly be serious sources of irritation to the delicate structure of the laryngeal and bronchial mucous membrane and to the substance of the lungs Several of the men complained of the dryness and dustiness of the mines in which they worked, and one man said that 'the dust was far worse than anything else they had to contend with'. So far, however, as I was able to judge I should doubt whether this cause generally acts very unfavourably upon the men, or at least whether it is comparable in its effects to other injurious influences. Portions of the lung of John Francis were subjected to careful chemical analysis by Dr Bernays, and no siliceous material was detected in them In the French millstone makers, to whose peculiar condition I have elsewhere drawn attention, there can be no doubt that the sharp particles of siliceous matter which they inhale do find their way into the lungs and become sources of serious irritation, determining, in persons of healthy constitution, broncho-pneumonic attacks which may ultimately lead to disorganization of the lungs, or in persons predisposed to consumption, true tubercular phthisis. The Cornish miners, however, probably like the gunflint makers of Meusnes in France, suffer more from the impure air which they breathe than from the inhalation of particles of stone." The Royal Commissioners of 1862 decided that dust was not a major factor in the production of the widely prevalent phthisis, but a Departmental Committee of 1902[18] investigating disease among the metal miners of Cornwall concluded that "it seems evident enough that stone dust which they inhale produces permanent injury of the lungs and that this injury . . . predisposes enormously to tuberculosis of the lungs"

The interrelation of silicosis and tuberculosis, which is still not understood, was fully recognized during the last century as the quotation in the last paragraph shows. Aldridge (1892) suggested that the tubercle bacillus is always inactive unless the lung is previously damaged by an agent such as dust· "Pathologists tell us of the presence of bacilli in tubercular disease, and favour the belief that these minute bodies are the cause of it. This belief may represent a whole truth, or only a partial one; in my opinion, the latter For I doubt if these bacilli actually develop phthisis unless there be

some antecedent change in the vitality of the affected tissue assuredly the breathing of dust may be reckoned as one (contributory factor) of no slight energy."

In this country the importance of pneumoconiosis as an industrial disease in the refractories industry was officially recognized in 1918 when Parliament passed the Workman's Compensation (Silicosis) Act under the Factory and Workshop Act. Four years earlier the British Royal Commission on Metalliferous Mines and Quarries (Second Report) classified quartz, quartzite, flint and sandstone as substances which, when inhaled, cause excessive mortality from respiratory diseases and especially from phthisis. These minerals were contrasted with coal, shale, slate, iron ore, clay, limestone, plaster of Paris and cement which were not thought to be responsible for any respiratory disease.

Once the serious nature of the disease was recognized precautions were taken by most industrial organizations throughout the world. Ventilation methods were generally improved and medical supervision was arranged. In at least one English firm a system of casual labour was adopted so that silica dust was not inhaled by any workman for more than a few months. In a few areas there was a refusal to recognize silicosis as an industrial disease. In France and Belgium, for example, a small but powerful group of mining companies and their medical advisers would not recognize the existence or the specificity of silicosis for some years. Martin[14] described their opposition in *La Médecine du Travail* which journal in 1937 devoted a whole issue to silicosis. The view forcibly stated there was that silicosis is different from tuberculosis, that it presents a different X ray picture, and that it is found only where quartz containing dust is inhaled.

In many industries enormous sums of money have been spent in combating the pneumoconiosis risk and in the payment of compensation. Some idea of the magnitude of the problem can be gained from the sums of money involved. The Rand gold mines paid £12 000 000 in compensation during twenty years in the early part of the century mostly to whites of whom about 15 000 were employed. Present day methods for the selection of labour and the frequent medical examination of personnel who are withdrawn from the mines at the first sign of trouble make it difficult to provide a comparable picture from more recent statistics.

The magnitude of the pneumoconiosis problem in different industries can be judged from Table 1.3. Table 1.4 gives the average age at death of persons reported to have died of pneumoconiosis contracted in several industries, and the number of years of employment in that industry

TABLE 1.3

Number of death certificates in which is recorded fibrosis of the lungs, including all forms of pneumoconiosis as well as byssinosis

	England and Wales, 1943–1952										Eng and Wales	Scotland
	1943	1944	1945	1946	1947	1948	1949	1950	1951	1952	1953	1953
SILICOSIS											PNEUMOCONIOSIS	
1 Retractories industries	7	6	9	8	10	13	13	8	8	11	6	3
2 Pottery, manufacture of	41	32	41	49	54	48	63	73	62	70	79	—
3 Sandstone, quarrying and dressing	24	26	21	20	12	28	15	10	33	9	23	—
4 Stone masons	53	31	44	41	43	40	36	19	38	23	21	1
5 Metal grinding	11	7	11	6	9	8	14	8	12	14	15	—
6 Sandblasting	6	7	6	4	5	5	5	3	3	1	3	—
7 Steel dressing and casting	4	10	5	22	13	13	18	11	6	11	10	8
8 Stone pebble flint and sand crushing	1	4	—	—	3	1	3	3	1	2	4	—
9 Scouring powders, manufacture of	1	1	1	—	—	—	1	1	1	1	—	—
10 Abrasive wheel manufacture	1	1	2	1	—	—	—	—	2	—	1	—
11 Glass cutting and bevelling	—	—	—	2	—	—	—	—	—	1	1	—
12 Millstone dressing	—	—	—	—	—	—	—	1	—	1	—	—
13 Slate quarrying and dressing	6	7	6	13	20	16	21	17	32	35	36	1
14 Granite quarrying and dressing	2	—	1	—	4	1	1	3	3	9	8	7
15 Tunnel mining (sewage works etc)	4	4	4	5	—	3	2	—	2	1	1	2
16 Coal-mining	276	277	323	343	347	322	336	337	347	339	1,016	240
17 Gold-mining (South Africa)	4	9	4	7	5	4	4	6	2	2	2	—
18 Tin-mining	14	11	19	14	12	11	20	9	4	17	18	—
19 Iron ore (haematite) mining	5	7	2	9	6	12	9	6	6	9	23	—
20 Lead mining	1	1	1	1	2	—	1	—	1	1	2	1
21 Copper mining	1	—	—	—	—	—	1	—	—	—	—	—
22 Barytes-mining	4	—	2	1	1	—	3	—	1	—	—	1
23 Clay-mining	1	—	1	—	—	—	1	1	—	1	—	—
24 Mining engineers	1	—	—	1	1	2	1	—	—	—	—	—
25 Miscellaneous	2	4	5	6	11	7	7	39	67	28	63	16
Total	470	445	508	553	558	534	575	555	631	586	1,332	280
ASBESTOSIS	8	10	11	16	15	15	17	12	18	12	14	1
PNEUMOCONIOSIS Coal-mining	—	34	64	78	230	317	420	509	590	573	—	—
Other industries	—	3	11	5	12	19	14	26	58	44	—	—
BYSSINOSIS	7	1	10	3	4	8	7	11	8	13	22	—
OTHER CASES OF (NON OCCUPATIONAL) FIBROSIS	493	531	529	568	616	651	554	679	732	677	687	16
GRAND TOTAL	978	1,024	1,133	1,223	1,435	1,544	1,587	1,792	2,037	1,905	2,055	297

The figures are based on information contained in death certificates as notified to the Registrar General

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TABLE 1.4

Fatal cases investigated up to the end of 1953

	Number of deaths	Average age at death	Duration of employment in years		
			Longest	Shortest	Average
SILICOSIS					
Pottery					
Silicosis	750	61.7	62.0	2.8	38.4
Silicosis with tuberculosis	501	56.2	67.0	5.0	34.7
Sandstone					
Silicosis	267	60.9	62.0	9.0	39.0
Silicosis with tuberculosis	229	57.5	58.0	5.0	37.4
Grinding of Metals					
Silicosis	123	59.5	61.0	14.0	35.9
Silicosis with tuberculosis	211	54.0	56.0	2.8	33.0
Sandblasting					
Silicosis	75	50.4	42.0	1.7	13.4
Silicosis with tuberculosis	99	46.2	46.0	2.0	13.1
Manufacture of scouring powders					
Silicosis	16	40.8	37.0	2.3	8.3
Silicosis with tuberculosis	6	40.8	12.2	2.0	7.0
Miscellaneous					
Silicosis	283	55.4	57.0	1.5	24.1
Silicosis with tuberculosis	249	51.6	50.0	0.7	24.8
TOTAL					
Silicosis	1 514	59.4	62.0	1.5	34.1
Silicosis with tuberculosis	1 294	54.4	67.0	0.7	31.2
ASBESTOS					
Asbestosis	230	49.5	48.0	0.5	16.6
Asbestosis with tuberculosis	87	40.2	33.0	0.8	11.4

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England and Wales, 1943–1952										Eng and Wales	Scotland
·943	1944	1945	1946	1947	1948	1949	1950	1951	1952	1953	1953
										Pneumoconiosis	
7	6	9	8	10	13	13	8	8	11	6	3
41	32	41	49	54	48	63	73	62	70	79	—
24	26	21	20	12	28	15	10	33	9	23	—
53	31	44	41	43	40	36	19	38	23	21	1
11	7	11	6	9	8	14	8	12	14	15	—
6	7	6	4	5	5	5	3	3	1	3	—
4	10	5	22	13	13	18	11	6	11	10	8
1	4	—	—	3	1	3	3	1	2	4	—
1	1	1	—	—	—	1	1	1	1	—	—
1	1	2	1	—	—	—	—	2	—	1	—
—	—	—	2	—	—	—	—	—	1	1	—
—	—	—	—	—	—	—	1	—	1	—	—
6	7	6	13	20	16	21	17	32	35	36	1
2	—	1	—	4	1	1	3	3	9	8	7
4	4	4	5	—	3	2	—	2	1	1	2
276	277	323	343	347	322	336	337	347	339	1,016	240
4	9	4	7	5	4	4	6	2	2	2	—
14	11	19	14	12	11	20	9	4	17	18	—
5	7	2	9	6	12	9	6	6	9	23	—
1	1	1	1	2	—	1	—	1	1	2	1
1	—	—	—	—	—	1	—	—	—	—	—
4	—	2	1	1	—	3	—	1	—	—	1
1	—	1	—	—	—	1	1	—	1	—	—
1	—	—	1	2	2	1	—	—	—	—	—
2	4	5	6	11	7	7	39	67	28	63	16
470	445	508	553	558	534	575	555	631	586	1 332	280
8	10	11	16	15	15	17	12	18	12	14	1
—	34	64	78	230	317	420	509	590	573	—	—
—	3	11	5	12	19	14	26	58	44	—	—
7	1	10	3	4	8	7	11	8	13	22	—
493	531	529	568	616	651	554	679	732	677	687	16
978	1 024	1,133	1,223	1,435	1,544	1,587	1,792	2,037	1,905	2,055	297

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Silicosis	73	50.4	42.0	1.7	13.4
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Manufacture of scouring powders					
Silicosis	16	40.8	37.0	2.3	8.3
Silicosis with tuberculosis	6	40.9	12.2	2.0	7.0
Miscellaneous					
Silicosis	251	55.4	57.0	1.5	24.1
Silicosis with tuberculosis	245	51.6	50.0	0.7	24.8
TOTAL					
Silicosis	1 514	59.4	62.0	1.5	34.1
Silicosis with tuberculosis	1,294	54.4	67.0	0.7	31.2
ASBESTOSIS					
Asbestosis	230	49.5	48.0	0.5	16.6
Asbestosis with tuberculosis	87	40.2	33.0	0.8	11.4

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According to Collis and Yule[21] the figures in the Report on the Occupational Mortality of Males (based on the 1921 census) show that, when deaths from all causes are considered, the general mortality rate among workers exposed to silica dust is considerably higher than that of the general population or that of workers in other comparable industries where the dust contains little free silica. As a basis of comparison for different groups, the number of persons of the general population in a particular age group which give 1,000 deaths is found. The same number of persons in other groups is then studied, the number of deaths giving the *Comparative Mortality Figure* (C.M.F.). Certain errors may occur; for example, sandstone workers may move to limestone quarries and "non-silica" dusts may contain a proportion of silica, but the figures show a sufficient contrast to suggest that these errors can be neglected.

ducing little free silica. Table 1.5 shows that the youngest section in both groups showed mortality figures below that of the general

TABLE 1.5

Comparative Mortality Figures (all diseases)
(Collis and Yule, *J. industr. Hyg.*, 1933, 15, 395)

Age group	Silica group	Non-silica group
20–24	965	872
25–34	1,310	879
35–44	1,870	928
45–54	2,200	979
55–65	2,222	1,016

Comparative figure for standard population at each age is 1,000

population. The section of age 55–65 in the non-silica group had a slightly higher C.M.F. than the corresponding age group of the

apparent that the mortality is considerably higher in any trade if silica dust is formed

TABLE 1.6

Comparative Mortality Figures (Respiratory tuberculosis only)
(Cox and Yule *J. Industr. Hyg.* 1933 15 395)

Age group	Silica group	Non silica group	Agricultural Labourers
20–24	1 244	661	777
25–34	1 635	700	800
35–44	3 232	1 057	475
45–54	5 426	1 447	454
55–	6 643	1 318	467

Comparative figure for standard population at each age is 1 000

TABLE 1.7

Comparative Mortality Figures (Silica and non silica groups)
(Cox and Yule *J. Industr. Hyg.* 1933 15 395)

	C.M.F.
SILICA GROUP	
Tin and copper mine underground workers not superintending staff	4 335
Potters (mill workers slip makers potters)	1 642
Earthenware china etc kiln and oven men and kiln setters and placers	1 830
Metal grinders	1 977
Sandstone miners and quarriers	1 644
Sandstone masons cutters and dressers	2 098
NON SILICA GROUP	
Brick and plain tile makers moulders etc furnace and crucible pot makers	926
Brick tile etc kiln and oven men	878
Iron ore mine underground workers not superintending staff (Staffordshire and North Riding Yorkshire)	792
Limestone miners and quarriers	918
Limestone masons cutters and dressers	1 197

Comparative figure for standard population is 1 000

With the changing pattern of industry, many new raw materials have been introduced in recent years Some of these are known to be

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Comparative figure for standard population at each age is 1,000

population The section of age 55–65 in the non-silica group had a slightly higher C.M.F. than the corresponding age group of the general population, but this age group of the silica group showed a C.M F. more than double that of the general population Table 1 6 compares the death-rate from respiratory tuberculosis in the silica

Silica may cause fibrosis in any part of the body, and assessment of the fibrogenic power of dusts has been attempted also by injecting suspensions into animals at sites other than the lung. The most successful experiments are those in which the dust is administered by intraperitoneal injection. Nodules may be formed in a number of positions in the peritoneal cavity but because they may be widely scattered and irregularly placed, assessment of relative damage is difficult. These difficulties of technique must be borne in mind when considering the experimental results.

For the proper interpretation of experimental evidence a considerable amount of data is necessary. Details of the number of particles, size distribution and mass concentration of the atmospheric dust or the injected sample must be known. A knowledge of the chemical and mineralogical composition of the dusts, their physical and especially their surface properties is also required. The effects of the dusts on the tissues are usually observed in histological sections to which one of the standard staining techniques is applied. Staining with haematoxylin and eosin is adequate to show a general picture of tissue damage, but a silver impregnation technique which stains reticulin brown and collagen black is outstandingly successful in emphasizing the fibrosing regions. The position of siliceous materials in sections can be demonstrated by incinerating a section on a slide and subsequently washing the ash with hydrochloric acid to remove mineral matter other than silica.[8]

Pneumoconiosis has been investigated experimentally only during the last thirty years, but it is during this period that knowledge in the sciences concerned has rapidly and continuously increased. No greater emphasis of this fact can be given than by a comparison of the chemistry of silicic acid as it was described by Gye and Purdy[9] in 1922 in their classical paper on silicosis with our present day knowledge. In this period the structures of silica and the silicate minerals have been elucidated, a great deal has been learned about the structures and properties of the proteins in general and knowledge of the processes involved in the formation of fibrous tissue has accumulated. Because of this rapid progress, it is essential to consider some modern concepts in several branches of science which touch upon the problem of pneumoconiosis.

Although it is known that pneumoconiosis can be caused by dusts other than silica, silicosis is the most widespread type of pneumoconiosis and it is the least complicated and most studied. Some other forms of pneumoconiosis such as coal miners' pneumoconiosis are probably silicosis which is modified by the presence of other dusts. For this reason most of this book is devoted to silicosis and the properties of silica and silicic acid are described in some detail.

capable of producing pneumoconiosis. Beryllium, for example, has proved to be highly dangerous when inhaled and, in a much smaller degree, talc and metallic aluminium have become suspect

In remarkable contrast to the tissue-damaging properties of these dusts is the apparently inert nature of certain others, such as carborundum and cement This statement must be qualified, however, since, although the weight of evidence supports the view that such dusts are harmless, occasional reports of cases have appeared in which pneumoconiosis is thought to be due to dusts of these substances. For example, a very severe case of pneumoconiosis which was apparently due to the inhalation of cement dust has been described [22] Since it rarely happens that a person has been subject to the action of only one simple, industrial dust throughout his working life, the interpretation of some of these data may, in some cases, be at fault Many workers change their occupation; and even in the same occupation the hazard may vary, sometimes without the knowledge of the worker One instance of this relates to the preparation of some special types of cement, when there may be a hazard due to the admixture of crushed calcined flint.

The study of the effects of dusts on tissues is complicated by peculiar experimental difficulties. Only limited deductions can be made from observations on men who have worked in dusty atmospheres since in no two cases is the degree of exposure the same. Silicosis in man usually develops over a number of years and it is impossible to measure the degree of exposure over such a period; indeed, because of the difficulties of dust sampling, it is not easy to obtain an adequate record of exposure—i e. particle count, mass concentration, differential count and analysis—even over a period of hours.

Inhalation experiments using animals applied to the study of the effects of dust are limited both because of the mechanical difficulty of maintaining dusty atmospheres at a pre-determined concentration and particle-size distribution over long periods, and also because laboratory animals are comparatively short-lived so that experiments can be seldom run for longer than two years Such experiments are usually carried out by administering far heavier doses of dust than are normally inhaled by men and consequently the picture of experimental silicosis is somewhat distorted.

Because of the variation between animals, it is impossible to ensure that an animal will inhale a standard amount of dust and the technique of intratracheal injection was introduced to obviate this difficulty. A suspension of the dust is injected rapidly into the trachea with a little following air to drive it into the lung.[23] Even by this procedure part of the sample is inevitably lost.

three forms are found naturally. Tridymite is formed when quartz is heated for a long time at about 1000° C. It commonly occurs therefore in silica bricks which have had prolonged use in furnaces. Cristobalite occurs in silica bricks which have been used over long periods at the temperature at which quartz begins to sinter. The three forms of silica differ in their ability to produce fibrosis.

Each crystalline form of silica exists in two modifications, that stable at the lower temperature being called the β and that at the higher temperature the α variety. The α and β forms are easily interconverted. The α-β transition temperature for quartz is 573°, for tridymite 120-160°, and for cristobalite 200-275°.

Silica melts to a colourless glass at about 1,600°, and when melted a part of the silica sublimes. The sublimate is a light, white powder consisting of extremely small particles. It is variously called 20-ångström silica, silica sublimate or silica condensate. This powder is much more readily soluble in water than is powdered quartz. It is difficult to bring about the crystallization of silica after it has been fused. It forms a glass, vitreous silica, which occurs naturally as the mineral obsidian.

Flint and kieselguhr (diatomaceous earth) are other natural forms of silica which are mainly amorphous. A certain amount of crystallization has occurred in some deposits. Kieselguhr has been formed from the skeletons of diatoms, minute plants which are capable of extracting traces of silica from water, and of incorporating the silica in their casing.

The crystalline forms of silica are all based on a unit in which four oxygen atoms are disposed at the corners of a regular tetrahedron at the centre of which is a silicon atom (Fig. 2.1). The tetrahedra are disposed to one another in such a manner that each oxygen atom is common to two tetrahedra (Fig. 2.2). This arrangement produces a lattice of interlinked infinite —Si—O—Si—O— spirals, an arrangement illustrated in Fig. 2.3.

There are considerable differences between the arrangements of the SiO_4 tetrahedra in the three varieties of crystalline silica, and the conversion of one variety into another requires the fission of Si—O linkages. This accounts for the difficulty of effecting such a conversion. The α and β forms of any crystalline form of silica differ but slightly in structure (Fig. 2.4) and the conversion of one form into the other involves little change. Quartz, unlike the other forms of silica, is optically active and the fact that laevorotatory α quartz is converted into β quartz without racemization emphasizes the ease of conversion.

Plates cut from quartz show ✓ piezo-electric properties, the quartz expands when a current is passed through it and a current is produced

CHAPTER 2

THE STRUCTURE AND PROPERTIES OF SOME INDUSTRIAL MINERALS*

In all the natural silicate minerals silicon atoms are joined through oxygen atoms to form chains, sheets or, in silica itself, three-dimensional lattices The bonds in the —Si—O—Si— structure are not easily broken, they are usually much stronger than other bonds which are present. When rocks are shattered, dust particles are formed mainly by cleaving the weakest bonds When the mineral is formed from —Si—O—Si— chains which are joined laterally by other groups, the dust is in the form of fibrous particles. If the mineral is constructed from two-dimensional sheets of silicon and oxygen atoms, the dust particles will have the form of plates or flakes

The several forms of free silica have a three-dimensional lattice of [illegible] is surrounded

in an industrial process depends, then, on the chemical structure of the materials handled

A fibrous dust is contrasted with quartz dust in Figs. 2.14 and 2.6.

Silica

Silica occurs free as rock crystal (almost pure quartz) and as sand, sandstone, quartzite, tripoli, tridymite, flint, opal, chalcedony and diatomaceous earth.

[illegible] the stable form

considerable alteration in the crystal structure, and consequently all

* See *Minerals for the Chemical and Allied Industries*, S J Johnstone, 1954, Chapman and Hall, London, and *Structural Inorganic Chemistry*, A. F. Wells, 1945, Oxford University Press.

substances quartz does not possess piezo electric properties after it has been fused One theory advanced to explain the production of silicotic tissue by quartz assumed that the piezo-electric property was responsible (Chapter 11)



Fig 2 5 Photomicrograph of dust from rock crystal (pure crystalline quartz)



Fig 2 6 Photomicrograph of dust from fused quartz

Quartz particles are stained purple by thionin and toluidine blue in histological sections [2] Those several microns in diameter appear deep purple smaller particles are only slightly stained

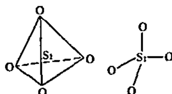


Fig 2 1 The structural unit of all forms of silica is a tetrahedral arrangement of four oxygen atoms around each silicon atom

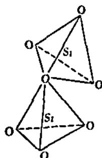


Fig 2 2 Two SiO_4 tetrahedra with a common oxygen atom

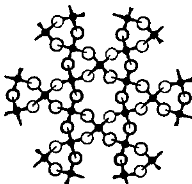
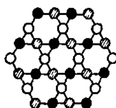


Fig 2 3 Plan of the structure of β-quartz. Small black circles represent Si atoms The oxygen atoms lie at different heights above the plane of the paper, those nearest the reader being drawn with heaviest lines Each atom is repeated at a certain distance above (and below) the plane of the paper along the normal to that plane so that the 3-membered rings in the plan represent spiral chains From Wells *Structural Inorganic Chemistry*.



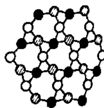


Fig 2 4 The arrangement of the Si atoms (in plan) in (a) β- quartz and (b) α- quartz.

when the quartz is squeezed. Such plates are used in multiple telephone lines, depth-sounding devices, and for the control of wavelength in radio transmitters Tridymite does not possess piezoelectric properties and, since the property is shown only by crystalline

As in quartz, the valency forces are approximately symmetrically disposed about every atom in the interior of silicon carbide crystals When a crystal is shattered, the dust particles which are formed have no one dimension which greatly exceeds any other A photomicrograph of carborundum dust is shown in Fig 2 8

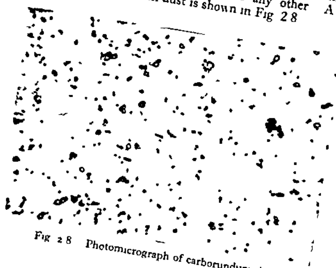


Fig 2 8 Photomicrograph of carborundum dust

Glass

When fused with calcium and potassium or calcium and sodium carbonates, silica gives glass, which is a supercooled silicate melt Other metallic oxides are sometimes added to give the glass special properties

Felspars

A quarter of the silicon atoms in the silica structure can be replaced by aluminium atoms This substitution of Al^{3+} for Si^{4+} results in a negatively charged structure which achieves neutrality by the addition of Na^+ or K^+ ions The resulting structures are those of felspars or zeolites Felspars occur widely as rock-forming minerals, that most commonly found being potash felspar $K_2O\ Al_2O_3\ 6SiO_2$ Microcline and orthoclase are different crystalline varieties of potash felspar Albite is a soda felspar, $Na_2O\ Al_2O_3\ 6SiO_2$ and oligoclase and labradorite are soda lime felspars Granites are composed of quartz and micas which are embedded in felspars Granite is very

The valency forces which hold the silica structure together are, approximately, equally strong in all directions; there is no plane of easy cleavage. Consequently a silica dust particle has no one dimension which greatly exceeds any other. When shattered, massive silica forms fine dust particles Dust formed from rock crystal is shown in Fig. 2.5 and from fused quartz in Fig. 2.6.

Carborundum

When mixed with coke and fused in an electric furnace at about 3,500°C, silica (sand) is converted into carborundum or silicon carbide (SiC) The carborundum forms large crystals, hexagonal plates, which are colourless and transparent when the carborundum is pure Three forms of carborundum are known. Their structures are built up by stacking units of carbon and silicon atoms in different [illegible] rounding

ious zone

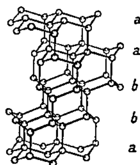


Fig 2 7 The structure of carborundum Alternate circles represent silicon and carbon atoms (Wells *Structural Inorganic Chemistry*)

Usually, silicon carbide is black and it gives a grey powder on crushing It is extremely hard, almost as hard as diamond, and it has a specific gravity of 3·2 It is not attacked by acids, it is inert even to hydrofluoric acid, but it is decomposed when fused with alkaline hydroxides Being refractory, it is used for making bricks for furnace walls It is used mainly as an abrasive.

The statistical composition of the kaolin minerals is $Al_2(OH)_4Si_2O_5$. The six positive charges of the aluminium atoms are balan... two negative charges of the ... charges of the hydroxyl ... kaolinite dickite and nacrite ...

Silicon in the silicon oxyg ... partly replaceable by aluminium ... apophyllite structure is replaced by aluminium Al^{3+} Each time a silicon ion Si^{4+} is replaced by aluminium Al^{3+} an additional positive ion is required by the structure This group constitutes the micas Thus from the apophyllite $Al_2(OH)_2Si_4O_{10}$ is derived the mica muscovite $KAl_2(OH)_2Si_3AlO_{10}$ Sericite sometimes called secondary white mica is very similar to muscovite It differs from m... that it contains less potass... m... rocks ... occur ... glome... mainl... degradation ... where it has been formed ... con elevated temperature and high pressure ... degradation of potash felspar under conditions of ... of clay minerals but contains mostly calcium montmorillonite ... Fuller s earth is a mixture

Talc

Talc is hydrated magnesium silicate having the theoretical formula $H_2Mg_3(SiO_3)_4$ Many specimens of talc have a structure which differs rather widely from that represented by this formula Similar minerals are known as soapstone steatite and pyrophyllite Soapstone is a soft greenish rock Pyrophyllite is a harder rock which unlike talc does not f... fol... rticles are usually ...

... such as serpentine tremolite anthophyllite ... degradation of other pyroxene Commercial talc may contain these minerals ... quartz may be present also and perhaps dolomite $CaMg(CO_3)_2$ and tremolite a calcium magnesium silicate Some of these impurities may be removed from the commercial product by air flotation The analyses of commercial talcs (Table 2...) ... siderable variation between ... compos...

Ir... the i... betw... ... the oxygen atoms so that the electrostatic ... occupies a large hole in the structure ... w con... in the ... Even in ... is only 1/12 The bonds between layers are easily broken and these minerals are characterized by their easy cleavage The micas

hard and when worked, as in quarrying and tin-mining, it must be drilled and blasted In these operations quartz is shattered and fine silica dust is produced.

Clays and Micas

The clay minerals are formed by the weathering of felspars *In silica, all the four oxygen atoms of each tetrahedral SiO_4 unit are* shared with other SiO_4 tetrahedra In the clays and micas only three oxygen atoms of each SiO_4 tetrahedron are shared with other

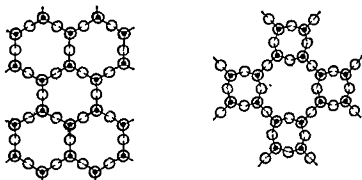


Fig 2.9 Two types of silicon-oxygen sheet (idealized) Oxygen *atoms lying above the Si atoms (small black circles) are drawn* more heavily From Wells *Structural Inorganic Chemistry*.

tetrahedra This arrangement results in infinite sheets of composition $(Si_2O_5)_n^{2n-}$ (Fig. 2.9) to which layers of hydroxyl groups are firmly cemented by magnesium or aluminium atoms (Fig. 2.10).

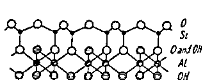


Fig 2.10 The composite layers of *the clay structure* From Wells *Structural Inorganic Chemistry*.

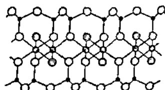


Fig 2.11. The composite layers of the apophyllite structure From Wells: *Structural Inorganic Chemistry*.

The process can be taken further to give a more complex structure having sheets of composition $Si_4O_{10}^{4-}$ (Fig. 2.11), a structure which occurs in the apophyllite group of minerals.

The statistical composition of the kaolin minerals is $Al_2(OH)_4Si_2O_5$. The six positive charges of the aluminium atoms are balanced by the two negative charges of the silicon oxygen unit and the four negative charges of the hydroxyl groups. Three kaolin minerals exist kaolinite, dickite and nacrite. Their structures differ only in detail.

Silicon in the silicon-oxygen sheets of the apophyllite structure is partly replaceable by aluminium. Each time a silicon ion, Si^{4+}, is replaced by aluminium, Al^{3+}, an additional positive ion is required by the structure. This group constitutes the micas. Thus, from the apophyllite $Al_2(OH)_2Si_4O_{10}$ is derived the mica, muscovite, $KAl_2(OH)_2Si_3AlO_{10}$. Sericite, sometimes called "secondary white mica", is very similar to muscovite. It differs from muscovite in that it contains less potassium, and more combined water. In rocks, it occurs in two forms, as minute plates and as fibres, muscovite occurs only as large plates. Sericite usually occurs in quartz conglomerates, sandstones and sandy shales where it has been formed mainly by the degradation of potash felspar under conditions of elevated temperature and high pressure. Fuller's earth is a mixture of clay minerals but contains mostly calcium montmorillonite.

Talc

Talc is hydrated magnesium silicate having the theoretical formula, $H_2Mg_3(SiO_3)_4$. Many specimens of talc have a structure which differs rather widely from that represented by this formula. Similar minerals are known as soapstone, steatite and pyrophyllite. Soap stone is a soft, greenish rock. Pyrophyllite is a harder rock which unlike talc, does not fuse when fired. Talc particles are usually foliated but fibrous varieties are known (asbestine).

Talc is of secondary origin, formed by the degradation of other magnesium silicates such as serpentine, tremolite, anthophyllite and pyroxene. Commercial talc may contain these minerals. Some quartz may be present also and perhaps dolomite, $CaMg(CO_3)_2$ and tremolite, a calcium magnesium silicate. Some of these impurities may be removed from the commercial product by air flotation. The analyses of commercial talcs (Table 2 [illegible]) siderable variation between sam[illegible] compo[illegible]

I[illegible] [illegible]w con

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[illegible]ctive oxygen atoms [illegible]ccupies a large hole in the structure [illegible] Even in is only 1/12. The bonds between layers are electrostatic bond strength minerals are characterized by their easy cleavage. The micas

TABLE 2 1

Chemical composition of commercial talcs (per cent)

	Best white talc, Luzenac, France	Second white talc, Luzenac, France	Grey talc, Norway	Best white talc, Mautern, Austria	Grey talc (soapstone) Miass, U S.S.R.	Superfine cosmetic talc, Italy	Grey talc, Johnson, Vt, U S A.	$H_2Mg_3(SiO_3)_4$ theoretical
Silica, SiO_2	61 00	57 00	38 40	61 54	58 93	60 34	42 73	63 5
Ferrous oxide, FeO	0 03	0 03	5 21	—	3 29	0 85	4 93	—
Ferric oxide, Fe_2O_3	0 84	0 99	0 91	0 76	0 29	0 23		—
Alumina, Al_2O_3	2 36	6·38	1 74	1·74	3 59	1·77	1 17	—
Lime, CaO	0 56	0 56	1 22	1 81	0 72	0 64	0 10	—
Magnesia, MgO	33 75	32 70	31 98	30 09	29 27	31 14	33 16	31 7
Soda, Na_2O	—	—	—	—	—	—	—	—
Potash, K_2O	—	—	—	—	—	—	—	—
Carbon dioxide, CO_2	nil	nil	16 26	3 65	0 50	0 78	4·74	—
Water above 105°C	1 03	1 83	3 58		3 08	5 20	12 95	4 8

This table is reproduced from *Minerals for the Chemical and Allied Industries* by S. J. Johnstone (Chapman and Hall, London)

cleave perfectly into parallel layers and dust particles are in the form of minute flakes Slate, another material which cleaves into thin broad sheets, is made up of mica (sericite or illite) and quartz It has been formed by the metamorphism of shales at high temperature and pressure

A series of minerals exists in which only two oxygen atoms of each SiO_4 tetrahedron are shared with other SiO_4 tetrahedra This arrangement results either in an infinite chain in the pyroxenes (Fig 2 12)

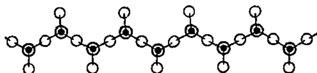


Fig 2 12 The silicon oxygen chain in the pyroxenes From Wells *Structural Inorganic Chemistry*

or in a closed ring (double chain) system (Fig 2 13) having the statistical formula $(SiO_3)_n^{2n}$

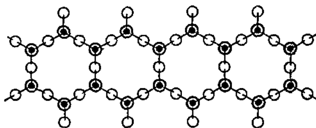


Fig 2 13 The silicon oxygen chain in amphiboles From Wells *Structural Inorganic Chemistry*

The [illegible]

morphous substitution is common in this group, for example, the total positive charge of tremolite, 14 corresponding to Ca_2Mg_5 is made up in soda tremolite by the ions $CaNa_2Mg_5$ Silicon atoms may be replaced by aluminium Thus hornblende contains the structure, $(Si_6Al_2O_{22})^{16-}$ The additional negative charges are

compensated by substituting aluminium atoms for magnesium atoms, or by adding extra alkali or alkaline earth metal atoms between the chains

Asbestos

Related to the amphibole group are the asbestos minerals. In the fibrous mineral chrysotile, $(OH)_6Mg_6Si_4O_{11}$, the metal ions are all magnesium and they are highly hydroxylated. The magnesium ions lie between the oxygen atoms of the Si_4O_{11} chains and the



Fig 2 14 An electron micrograph of a thermal precipitator sample taken from the air of an asbestos works Note, one dust particle is 5 μ long and only 0 02 μ thick. (Crown Copyright)

hydroxyl groups In effect, the chains are thus coated with hydroxyl groups and the binding of the chains is by these weakly-attracting [illegible] metal ions, as in the pyroxenes and [illegible] is minerals [illegible] uble, silky ibres which can be woven into fabric. It usually contains some iron

and aluminium. The fibres lose water and become brittle if heated above 450°.

Even when broken up into dust particles, chrysotile largely retains its fibrous form. A remarkable electron micrograph of an asbestos fibre which was collected from the air of an asbestos mill by a thermal precipitator is seen in Fig. 2.14. Its length is 5 μ but its thickness is only 0.02 μ, that is, too small to be visible when viewed under an optical microscope.

Besides chrysotile, other important asbestos minerals are crocidolite, amosite, anthophyllite, tremolite and actinolite.

Crocidolite is blue asbestos. It has the chemical composition $H_2Na_2Fe_5Si_8O_{24}$. It comes from the Cape and Transvaal almost exclusively. Crocidolite is difficult to weave and is used mainly as a thermal insulator.

Amosite resembles crocidolite chemically. It exists as grey fibres up to 12 inches long which are flexible and have a high tensile strength. It is brittle and difficult to spin.

Anthophyllite is brittle and of poor tensile strength. It is used mainly in asbestos paint.

Tremolite, a magnesium calcium silicate, occurs as long white silky fibres of poor strength. It is unsuitable for spinning.

Asbestos minerals are decomposed by acids, even by very weak acids such as acetic and carbonic acids. Leitmeier[28] shook 1 g serpentine in 100 g water at room temperature in the presence of carbon dioxide. After 6 months he obtained the following analysis of the solid and the solution.

Solution	(g. 100 ml.)
MgO	3.07
FeO	0.38
SiO_2	0.23
	3.68

Residue	(g./100 g.)
MgO	33.64
FeO	9.64
CaO	0.28
Al_2O_3	0.32
SiO_2	39.72
H_2O	12.86

CHAPTER 3

THE CHEMISTRY OF THE SURFACES OF MINERALS

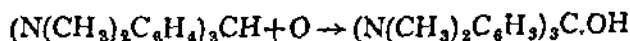
Whatever the mechanism of fibrogenesis in pneumoconiosis, whether it be due to the solution of dust particles in the tissue fluids, the direct action of the particles on the tissue or the adsorption of plasma constituents on to the dust particles, it is primarily the surface of the dust that is involved.[30] As the size of a particle is reduced, the ratio of the surface area to the mass increases When small particles are considered, as in the study of air-borne dusts, any difference between the composition and properties of the surface and those of the bulk material may become significant.

The structures which were discussed in Chapter 2 are those of the bulk minerals; the statistical composition was considered and an infinite lattice was assumed. If the lattice is fractured, the valency forces which previously held the parts together are now unsatisfied and the freshly-formed surfaces are highly reactive

The atoms in these surfaces will rapidly combine with any adjacent molecules. Under normal conditions when a mineral is fractured the active surfaces react with the oxygen or the water vapour of the air; usually the surface is assumed to consist of hydroxyl groups [illegible] different from the

surface first react with oxygen, a strongly oxidizing surface results.

Examples of this action have been described.[31] When dried quartz is ground in a pestle and mortar with the colourless dyebase *hexamethyltriaminotriphenylmethane, the latter is oxidized* to the leuco-base of methyl violet which gives an intense colour on acidification.



$$(N(CH_3)_2C_6H_4)_3CH+O \rightarrow (N(CH_3)_2C_6H_3)_3C.OH$$

The oxygen of the air is necessary for this reaction; it does not occur when the quartz is ground under benzene.

The surface of a quartz particle

When a quartz crystal is fractured, free valency forces must be associated with both silicon and oxygen atoms in the surface. This

state is represented diagrammatically in Fig 3 1 The freshly formed surface reacts with moisture to produce a surface of hydroxyl groups Fig 3 2 These hydroxyl groups will react like those in silicic acid itself, the surface acts as a weak acid and the hydrogen atoms may be replaced by, for example, sodium ions

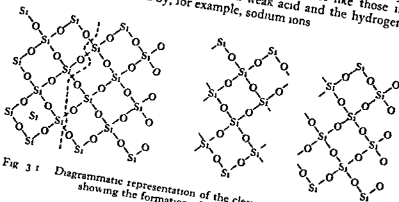


Fig 3 1 Diagrammatic representation of the cleavage of a quartz crystal, showing the formation of an active surface

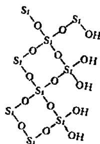


Fig 3 2 Diagrammatic representation of a hydrated quartz surface

Silica which has been in contact with moisture has also a layer of silicic acid on its surface This layer is removed if the silica is treated with sodium hydroxide The following evidence for the presence of silicic acid has been described 32 When silica is added to water or to dilute alkali, the concentration of the dissolved silicic acid increases rapidly at first After some time the rate of solution is reduced and the silica dissolves very slowly The form of the solubility curve is discussed in detail in Chapter 5, but it may be stated here that the phase of rapid solution represents the dissolution

of the adsorbed silicic acid and that the slow phase corresponds to the attack of the water on the silica lattice.

There seems to be some doubt as to whether there exists yet another type of differentiation between the surface and the interior of quartz particles. By X-ray diffraction methods, Nagelschmidt, Gordon and Griffin[33] have given evidence for a thick, disorganized layer which resembles the Beilby layer on the surface of polished metals Clelland and Ritchie[34] have also suggested this. No such layer could be detected by electron diffraction methods.[35]

The surface of a silicate mineral

The considerations which have been applied to quartz will apply also to other mineral silicates; the position is complicated, however, because of the diversity of the atoms and groups which are present We have seen that in the case of many silicates there are planes of weakness in the solids which become cleavage planes. Very often cleavage along one of these planes will leave a relatively inactive surface because the parts of the molecule were held together only by weak forces. Many minerals, however, show the same highly reactive surfaces on grinding as does silica. The colour reaction described earlier which is given when silica is ground with hexamethyltriaminotriphenylmethane and which is thought to be due to adsorbed oxygen is given when a number of other minerals are ground with this base. Halloysite, $Al_2O_3\,2SiO_2H_2O$, sodium montmorillonite, $(Na)_2O\ Al_2O_3.5SiO_2\ nH_2O$, and leucite $KAl(SiO_3)_2$, give this reaction.[36] The inactivity of gibbsite $Al_2O_3.3H_2O$ and brucite $MgO\ H_2O$ indicates that the reaction is not due to hydroxyl groups as such Among the clay minerals, the colour reaction is invoked only when at least one surface of the structure is composed of silica Colour reactions which occur between clays and organic amines are now believed to be due to the oxidation of the amine by

[illegible]

e will result in a relatively
a different plane, and this
must occur to some extent in the formation of dust particles, a more reactive surface will be formed. In some cases this results in the *liberation of metal ions* Asbestos provides an example of this. Whilst the composite fibres are held together by weak forces and their separation leaves an "inactive" surface, cleavage of the structure in a plane perpendicular to that of the fibres leaves more powerful valency forces unsatisfied. If native asbestos is teased into loosely separated fibre-bundles and a bundle is cut transversely, then embedded in an agar jelly containing phenolphthalein, the indicator becomes pink only in the vicinity of the ends of the fibres where

active surfaces produce magnesium hydroxide This effect may be responsible for the peculiar shape of the asbestosis bodies found in

demonstrated by fracturing glass Phenolphthalein in aqueous alcohol will remain colourless indefinitely in a test tube made from

dusts proved that it was largely hydrated, several per cent of its weight consisting of combined water, some of which was not lost when the dust was heated to 800° Granite evolves only about 0 5 per cent water when heated to 1,000–1,400° [39] The reaction at the particle surfaces is similar to the natural changes which take place in the composition of rocks, known geologically as weathering, which result in the formation of hydrous, mica-like minerals

These observations of some minerals show that the surface has a different composition from that of the bulk But apart from these qualitative results little is known about the surface of minerals because it is difficult to devise direct methods of investigation X-ray diffraction, which has been so successfully applied to the examination of the crystal lattice, is inapplicable, it can be used only when the lattice is 10^{-1} to 10^{-2} mm thick Electron diffraction, as usually applied to the study of "surfaces", yields information about the fifty or so layers in the surface Knowledge of the single outer layer can be obtained only indirectly

Infra-red studies have been used to demonstrate the hydration of the surface of other siliceous minerals [36] For example, sodium montmorillonite at 25° shows a relatively sharp band near 3,700 cm $^{-1}$, characteristic of hydroxyl as found in hydroxides and water vapour, as well as the broad band from 3,200 to 3,600 cm $^{-1}$, characteristic of liquid water On heating the latter band almost disappears but the

former band persists The same is true for hydrogen montmorillonite, obtained by dialyzing sodium montmorillonite which carries hydrogen as a counter ion.

Differential thermal analysis[36] of a number of siliceous minerals shows that there is an initial endothermic peak about 140° which also is attributed to adsorbed water. The magnitude of this peak and, therefore, the amount of adsorbed water, depends on the surface area of the sample

It seems likely that some of the methods of investigation which have been applied to silica could also give information about the surface of silicate minerals. In particular, the rates of solution of all the elements present and the rates of exchange of isotopically labelled elements with the elements in the lattice might be followed. The potentiometric titration of the dusts could give information about the surface hydroxyl groups It seems probable that in some cases metal ions which are deep in the lattice may be removed by leaching with water.

The surface of carborundum

There is abundant evidence that carborundum surfaces are often coated with some other material[40]. A monolayer of adsorbed silicic acid was detected on a silica surface by studying the rate of the dissolution of the silica in water or dilute alkali. The same method has been used to examine the surface of carborundum particles. Like silica, carborundum dissolves rapidly at first, but the rate of solution (followed by measuring the dissolved silica) is considerably reduced after a time There are two breaks in the solubility-time curve, which suggests again, that there is adsorbed silicic acid at the surface. It seems likely that the surface of carborundum is identical with the surface of silica, that there is a layer of —SiOH groups and on to this layer silicic acid is adsorbed.

This conception of the carborundum surface agrees with measurements made of the ionic adsorption energies of various ions from solution on to carborundum surfaces. The values of these are strikingly similar to the values obtained for silica particles.

Some years ago it was observed that there was a layer on the surface of a carborundum crystal which was different from the bulk of the material. Electron diffraction patterns made by a carborundum plate show diffuse halos.[41] If the surface of the crystal is abraided with emery, sharp diffraction patterns are produced. Since emery is softer than carborundum the layer removed from the surface cannot be carborundum Finch and Willman[42] suggested that it was silica. Hydrofluoric acid and sodium hydroxide are also effective in producing a surface which gives sharp diffraction patterns.

A crystal from which the surface has been removed by such treatment and which gives sharp patterns can again be made to give diffuse patterns by heating it in a bunsen flame Finch calculated that the silica layer is not more than 43 Å thick

From this evidence it would appear that the surface normally presented by carborundum is similar to that normally presented by silica This observation is important because the fibrogenic activity of silica is very different from that of carborundum

CHAPTER 4

THE CHEMISTRY OF SILICIC ACID

The solubility theory of silicosis, which has been advanced to explain the effect of silica dust on the lung tissues, assumes that silicic acid is the direct pathogenic agent. The chemistry of silicic acid has been studied in detail only during the last few years and the work which has been published is not well known. In some cases this chemistry throws new light on the experimental work which was undertaken to confirm the Solubility Theory, and sometimes it shows that the interpretation of these experiments was incorrect

When a solution of sodium silicate in a concentration of, say, one per cent is acidified with hydrochloric acid only a part of the silicic acid solution which is formed will pass through a semipermeable membrane of parchment or "Cellophane". Whether or not a

silica and Cellophane are negatively charged, the maximum molecular weight of the silicic acid which will penetrate the membrane is probably below this value The separation of the sol into a diffusible and a non-diffusible fraction shows that the silicic acid is partly in the form of complex polymers of high molecular weight, and partly as smaller particles Fresh silicic acid sols, prepared by the addition of hydrochloric acid to sodium silicate solutions, contain smaller polymers which are not precipitated by egg albumin or methylene blue. These sols, originally called α-silicic acid, are converted by polymerization on standing into a form (β-silicic acid) which is precipitated by these reagents [44]

Orthosilicic acid

The earliest systematic study of the *properties of silicic acid* was made in Wilstätter's laboratory. In his work on the structure of

chlorophyll, Wilstatter used the process of adsorption on to silica gel to purify his extracts and, so that he should better understand this procedure, he carried out simultaneous research on the structure and properties of silica and silicic acid. The existence of simple orthosilicic acid molecules, $Si(OH)_4$, was demonstrated by Wilstätter, Kraut and Lobinger[45, 46, 47] who, from silver oxide paste and silicon tetrachloride, prepared a silicic acid which had a molecular weight, as determined by freezing-point measurements, corresponding to the monomer. Saponification of tetraethylorthosilicate gave a silicic acid which had an initial molecular weight approximating to that of the dimer. Because these solutions were contaminated by other ions, and because the freezing-point depressions were very small, the molecular weight values must be regarded with some reserve, but it is true that the silicic acid particles in the solutions must have been small.

The simple orthosilicic acid has also been prepared by Gruner and Elod[48] and more recently by Weitz and Franck[49] and by Alexander[50]. Alexander's method is to stir powdered sodium metasilicate into an aqueous slurry of a cationic exchange resin in the hydrogen form at 0°C at a pH below 3.5. The monomer is stabilized by a trace of acid (pH 3). Rather more complex silicic acids are formed if the metasilicate is added as a solution but the simple acid may be prepared from either solid or aqueous sodium orthosilicate.

Polymerization

None of the simple silicic acid solutions is stable except when very dilute or at a low pH. Polymerization commences immediately the solution is prepared. For example, cryoscopic and conductivity measurements made on a solution produced by the action of hydrochloric acid on sodium silicate at 0°C, indicated an average molecular weight for the silicic acid of 155. On standing or warming, the average molecular weight increased to about 50,000.[51] Sols containing highly polymerized silicic acid are slowly depolymerized if they are diluted and made acid, say pH 2-4,[52] or alkaline.

The process of polymerization can be demonstrated in another way. When silicic acid sols, prepared by acidifying a sodium silicate solution, are dialyzed through a collodion membrane, the amount which will pass the membrane in a fixed time interval depends on the time elapsing after the preparation of the sol.[53] This is evident from Fig. 4.1 which shows the weight of silica passing a membrane in ten minutes, dialysis commencing at different intervals of time after the preparation of the sol. A small amount of silica will dialyze even from a silicic acid gel, indicating that simpler silicic acids remain in equilibrium with the larger polymers.

At pH values near 6, silicic acid sols gel rapidly on storing if they are more concentrated than about 1 per cent. Even sols containing only 0·3 per cent SiO_2 will flocculate in one or two days. The rate of polymerization and gelation is governed by a number of factors including concentration, temperature and pH. Neutral salts and many other substances have also been shown to affect the rate.

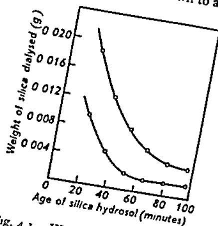
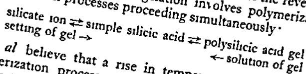


Fig. 4.1. Weight of silica dialyzing from two silicic acid sols in a fixed time, plotted against the age of the sol (Hurd and Merz, *J. Amer chem. Soc.*, 1946, 68, 61).

The variation of the rate of polymerization as affected by the factors mentioned has been adequately studied only for silicic acid sols of concentration greater than about 0·2 per cent The rate increases with the concentration Gel formation is accelerated by increased temperature at pH values below 10,[54, 55, 56, 57] but the reverse is true between pH 10 and 11. If gelation involves polymerization and depolymerization processes proceeding simultaneously·



Hurd *et al* believe that a rise in temperature may accelerate the depolymerization process to a greater extent than it accelerates polymerization.[58]

A change in pH has been noted during gel formation in alkaline and strongly acid solutions No such changes have been observed in sols near pH 7 but all the sols examined were strongly buffered. The pH change is taken to indicate that the more complex silicic

before and after supersaturated (1 5 g SiO_2/100 ml) solutions of orthosilicic acid had stood for 6 months at 25°C

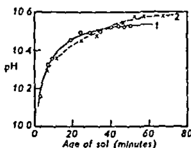


Fig 4 2 Change of pH accompanying the gelation of a sol in the alkaline range (Hurd, Pomatti Spittle and Alois *J Amer chem Soc*, 1944 66, 388)

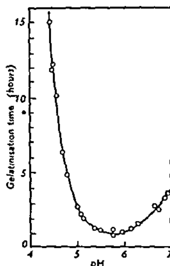


Fig 4 3 Time required for gel formation in silicic acid sols at different pH values (Treadwell, *Trans Faraday Soc*, 1935 31, 298)

The rate of polymerization of a silicic acid sol depends largely on the pH Treadwell[66] who measured the time required for gel

Freundlich and Cohn[408] gave the value 9 5 to 11, Ray and Ganguly[410] 6 to 8 Batchelor[39] 6 5 to 7 5, Hurd and Barclay[67] 8 3 and Merrill and Spencer[411] 7 to 8

Silicic acid polymers of high molecular weight do not react with ammonium molybdate to give a yellow colour, a reaction which is

characteristic of smaller silicic acid polymers (oligo-silicic acids). Alexander, Heston and Iler's[52] method for the estimation of monosilicic acid and "molybdate-reactive" silicic acid uses a solution containing 100 g. of ammonium molybdate, $(NH_4)_6Mo_7O_{24}.4H_2O$), in 1 litre of solution. Their reagent is prepared immediately before use by adding 40 ml of this solution to 860 ml. distilled water and acidifying with 100 ml N-sulphuric acid. After the reagent is added to the silicic acid sample, the colour density of the solution at a wavelength of 400 mμ is measured at ½-minute intervals at 25°C until it becomes constant. All the monosilicic acid reacts within 2 minutes. The colour which develops afterwards is due to reactive polymers.

Studies[49] of the polymerization of silicic acid using the molybdate reaction indicate that the conversion of monosilicic acid into the oligo- and then into the polysilicic acids is reversible. The position of the equilibrium and the rates of the forward and back reactions depend on pH. The rates are slowest at about pH 3. An increase in temperature results in depolymerization of the acids. No change in the molybdate-reactive silicic acid could be detected when a freshly-prepared 0·001 M solution was allowed to stand,[59] suggesting that solutions of this concentration do not polymerize. A reduction in the amount of molybdate-reactive silica was noted when more concentrated solutions were allowed to stand (Table 4.1).

The polymerization of silicic acid is accelerated by neutral salts, such as sodium chloride. Sols containing 1 per cent SiO_2 are stable

TABLE 4.1

Molybdate Reactive SiO_2 *in 25 ml. solution (mg)*

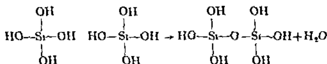
SiO_2 concn	0 001M	0 005M	0 01M	0 05M
After time				
1 hr	0 300	0 303	0 307	0 300
3 hr	0 300	0 294	0 235	0 146
24 hr	0 300			
7 days	0 300			
	0 302			
Reduction after 3 hr	0	0 009	0 072	0 154

for long periods if salts are removed by dialysis, but such sols may gel almost instantaneously after sodium chloride is added. Sols prepared by the electrodialysis of sodium silicate in the complete absence of other salts show remarkable stability. Even at 5 per cent concentration they may not gel for several days. Polymerization is retarded by polyhydric alcohols such as glycol, glycerol, mannitol and starch and by gelatin. Monohydric alcohols are ineffective.[60]

Polysilicic acids form precipitates with egg albumen. Precipitates are not formed until a certain degree of complexity has been reached. Solutions containing N/20 and N/125 hydrochloric acid give no precipitate until the average molecular weight of the silicic acid has reached about 300. A solution containing N/625 hydrochloric acid, however, gives a precipitate when the average molecular weight has reached about 200.[60] The latter solution probably contains more complex polymers even though the average molecular weight is smaller.

Chemistry of polymerization

The polymerization of silicic acid sols is generally regarded as due to the condensation of silicic acid molecules.[61] In the simplest case, two molecules of orthosilicic acid combine thus



Further polymerization will give straight or branched chains or networks. Long chains are considered to be less probable than irregular networks both because no double refraction has been observed in flowing sols and because a silicic acid sol requires a long time to establish temperature equilibrium at its freezing point. This last property is associated with decreased mobility which would

and silicate structures are derived by linking SiO_4 tetrahedra similar principles should be applied to the constitution of colloidal silica'[61] At the surface of the particle, oxygen atoms which are bound to only one silicon atom are negatively charged or silicon atoms lacking an oxygen atom are positively charged. These charges are satisfied by protons or hydroxyl ions derived from water. As the O—H bond is weaker than the Si—O bond, protons may separate, and the surface may accordingly act as a very weak acid.

On this view of the structure of silicic acids the hydration of polymers is confined to the surface and the degree of hydration is a function of the surface area and, therefore of the particle size. The smallest silica particle has the structure $Si(OH)_4$ and, since the smallest particle is completely hydrated, there can be no metasilicic

acid, H_2SiO_3 The formula for sodium metasilicate usually written as Na_2SiO_3 should be written as $Na_2H_2SiO_4$.

Weyl and Hauser[62] discuss several stages in the formation of silica gel and assume that it is due to a change in the co-ordination number of silicon from four to six. Because the proton is small, when accompanied by an electron it can penetrate into the outer electron shell of an oxygen ion (O^{2-}). This has the same effect as an increase in the nuclear charge and causes the electron cloud to contract. This explains why the OH^- ion is small enough to be interchangeable with the fluoride ion in minerals such as mica and

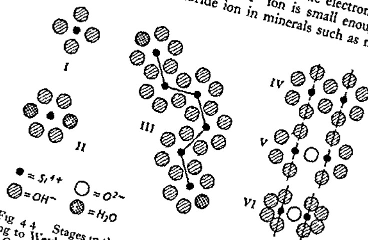


Fig 4 4 Stages in the polymerization of silicic acid, according to Weyl and Hauser (*Kolloid-Zeitschrift*, 1951, 124, 72) I Orthosilicic acid, $Si(OH)_4$, molecule II Orthosilicic acid with two co-ordinated water molecules. III Polymerization IV Adjacent groups in the polymer. V Condensation. VI Syneresis.

apatite Just as four F^- ions are insufficient to screen the Si^{4+} ion so that SiF_4 is chemically unsaturated and surrounds itself with four more F^- ions in the fluosilicate ion, $—SiF_6^{2-}$, so $Si(OH)_4$ is unsaturated In alkaline solution effective screening is provided by two OH^- ions, giving the silicate ion $Si(OH)_6^{2-}$, equivalent to $SiO_3^{2-}.3H_2O$. In neutral solution the initial screening by H_2O dipoles is less effective and is replaced by screening provided by other silicic acid molecules which are more highly polar. A later stage of condensation is pictured between the six co-ordinated molecules These stages are represented two-dimensionally in Fig 4 4.

According to recent work[63] the polymerization of silicic acid does not involve condensation at all The constitution of polysilicic acid,

as a sol or as gelatinous silica, is that of a mass of co-ordinated orthosilicic acid molecules represented as III in Fig 4 4 Condensation probably occurs only if the silicic acid is heated to a temperature of several hundred degrees This view accords with many of the observed properties of polysilicic acid

Acidic properties of silicic acid

Although there is little doubt that silicic acid is, in fact, an acid, much of the data describing its acidic properties is inconsistent The pH of repeatedly washed gelatinous silica was found to be 6 5 by Bradfield,[64] but Kargin and Rabinowitch[65] gave the value as 7 0 On the other hand, the electrodialysis of sodium silicate, which is equivalent to its hydrolysis and leaves colloidal silica in electrolyte-free water, produces a sol of pH 3 2 [66] It has been claimed[67, 68, 69] that the larger polymers of silicic acid are relatively strong acids, considerably stronger than orthosilicic acid, others[70] claim that large and small polymers are of similar strength Kargin and Rabinowitch,[65] who reviewed the work up to 1936, have suggested that the high acidity claimed by some for silicic acids is due to insufficient purification, most specimens being contaminated with hydrochloric acid The pK values for the first and second dissociations of silicic acid have been given as 9 5 and 11·7,[71] 10 and 12,[67] and 9 7 and 12 [66]

Sodium Silicate

When sodium hydroxide is added to a silica sol, protons of the surface hydroxyl groups are replaced by sodium ions These cannot closely approach the oxygen atom, however, and they remain as a diffuse, positive "counterion" layer around the surface of the negatively charged silica A sharp rise in pH is observed as soon as the protons of the surface hydroxyl groups are replaced However, if sodium silicates are prepared by fusing together silica and sodium hydroxide, the free hydroxyl concentration of their solutions are very small, at least between the SiO_2 Na_2O ratios of 4 1 and 1 1 In the process of fusion —Si—O— linkages are broken by the action of the sodium hydroxide so that the silicate particles are smaller as the SiO_2 Na_2O ratio is reduced

If powdered silica is fused with sodium hydroxide or sodium carbonate, a clear melt is formed which is slowly soluble in water Solutions of sodium silicate of any strength can be prepared If the ratio of Na_2O SiO_2 is 1 1, a solution of the melt will produce crystals having the empirical composition $Na_2O\ SiO_2\ 2\,(6 \text{ or } 9)\,H_2O$ This "hydrated metasilicate" dissolves in water to give a clear solution.

Even sodium silicate solutions may contain polymeric anions. Sodium silicate (1·35 N) has been shown to dialyze completely through collodion membranes,[73] the dialysate giving only a faint Tyndall cone. This observation does not necessarily mean that no large polymers are present in the solution since complete dialysis would also be expected if polymers are present but are in equilibrium with smaller ions.

Evidence for the presence of material of colloidal size in concentrated sodium silicate solutions has been provided by Cann and Gilmore[72] who found that boiling point elevations are less than those required for solutions of the simple silicate when the $Na_2O \cdot SiO_2$ ratio is 1.3·75. Viscosity measurements and Tyndall beam studies [97, 98] have also indicated that colloidal particles are present in these solutions when the $Na_2O:SiO_2$ ratio is 1:3.

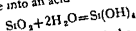
Naumann and Debye[73] prepared sodium silicate solutions of high purity which they filtered through sintered platinum. In the Tyndallometer, these solutions were found to contain small particles even when the $Na_2O \cdot SiO_2$ ratio was as high as 1:3·75. Sodium silicate of $Na_2O . SiO_2$ ratio 1:2 behaved like cane sugar; the solutions showed no evidence of polymerization. When the proportion of SiO_2 was higher, there was always evidence of polymerization and the degree of aggregation was proportional to the concentration of the solution.

Half a century ago Kohlrausch[74] from conductivity measurements of solutions of silicates having the compositions $Na_2O.SiO_2$ and Na_2O 3·4SiO_2 concluded that sodium silicate is at least partly hydrolyzed in solution. About the same time Kahlenburg and Lincoln[75] deduced from freezing point data that sodium silicate in a concentration of 1 gram molecule in 48 litres is completely hydrolyzed into sodium hydroxide and colloidal silica.

CHAPTER 5

THE SOLUBILITY OF SILICA AND SILICATES

The theory that tissue damage in silicosis is due to silicic acid formed by the dissolution of silica in the tissue fluid, which is discussed in Chapter 11, led to extended studies being undertaken on the rates of solution of siliceous dusts and powders. Before this theory had aroused interest in the process of dissolution of silica, the solubility of quartz had been studied only from the viewpoint of geological and analytical chemistry. The action of water on other siliceous materials has still received little attention. Silica dissolves very slowly in water. The dissolution is a chemical reaction, the conversion of an oxide into an acid



$$SiO_2+2H_2O=Si(OH)_4$$

The process is, however, complex and the system has yet to be adequately studied.

Some of the most careful measurements of the solubility of gelatinous silica and of quartz were made by Lenher and Merrill[76]. They extracted the silica with water in apparatus made entirely in platinum, and they estimated the silica in the solute gravimetrically. They obtained absolute solubility values for gelatinous silica of 41.8 mg SiO_2 in 100 ml in conductivity water at 90°C, and 16.2 mg SiO_2 in 100 ml at 25°C. Equilibrium was established after 24 hours at 90° or about 8 days at 25°. After ignition the rate of solution of the silica is reduced. Lenher and Merrill said, "the true solubility of ignited silica is probably the same as that of gelatinous silica, but as saturation is not reached in any short period of time, the apparent solubility is somewhat less than that of gelatinous silica."

Alexander, Heston and Iler[52] recently re-examined the values for ... ater. Measuring the solute concentration ... phous silica produced ... sols produced by ... approxi- ... nd ... for ... other forms of silica are

silica gel; for example, Briscoe, Matthews, Holt and Sanderson[77] found that, when 1 g. of quartz dust was agitated with 100 ml. of water at 20°, the solute contained only 1·6 mg. SiO_2 per 100 ml after 50 days.

But various workers have found it impossible to obtain an equilibrium between silica and water within a reasonably short time. For this reason extractions have been made to compare the amount of silica which passes into solution from different samples of silica after an arbitrary length of time and using arbitrarily chosen conditions. Some of this data is given in Table 5.1.[78] Some extractions were made with water as the solvent but, to more nearly approach the conditions of the body, other extractions were made using serum or ascitic fluid. Ascitic fluid is similar to serum and lung fluid except that it contains much less protein

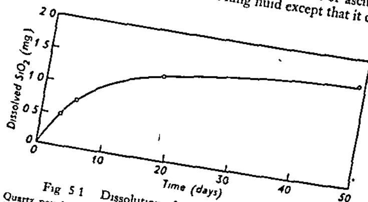


Fig 5 1 Dissolution of quartz in water, at 20°C

Quartz powder (1 g, particle size mainly 1–3 µ) was extracted with water (100 ml). The mass of the dissolved silica is plotted against the time of extraction (Briscoe, Holt, Matthews and Sanderson *Trans. Instn Min Metall*, 46, 291, 1936–7)

The rates of solution of various forms of silica have also been studied by, for example, Briscoe, Holt, Matthews and Sanderson[77] and Lucas and Dolan [78] It is generally agreed that, when powdered silica is added to water and the concentration of the dissolved silica is plotted against time, the curve shows an initial phase of rapid solution after which the silica dissolves much more slowly. "All sizes of quartz particles behaved as if a soluble fraction of silica was being leached from their surfaces, leaving a relatively insoluble residue, or core, which seems to be resistant to the dissolving action of water The amount of leachable silica which can be dissolved from the particles is greater with the samples of small size quartz than with those of larger size" (King [84]) A typical solubility curve is shown in Fig 5.1. If the extraction of the quartz is con-

TABLE 5.1

Dissolution of Silica in various fluids

Form of silica	grams solid per 100 ml	Diss. SiO_2 mg per 100 ml	Solvent	Exposure	Temp °C	Author and method
AMORPHOUS						
Gelatinous	2*	9.0	Serum	1 week	37	Ultra-centrif
Gelatinous	2	9.1	Ascitic fluid	72 hours	37	Ultra-centrif
Dry	2.5	10	Water	10 days	37	Colorimetric
Desiccated	2	7.0	Ascitic fluid	8 days	37	Ultra-centrif
Fresh	2	9.0	Ascitic fluid	8 days	37	Ultra-centrif
Fresh	2.5	14	Pleural fluid	10 days	37	Colorimetric
QUARTZ						
Quartz	1	3.3	Water			Colorimetric
	4	3.8	Water	8 days	37	Colorimetric
	1	5.2	Water	8 weeks	20	Colorimetric
	0.01	0.05	Water	3 hours	100	Ultra filtr
	1	4.3	Water	2 months	37	Colorimetric
		5	Water	10 days	37	Colorimetric
	3	19	1 per cent $NaHCO_3$	48 hours	37	Colorimetric
	3	18	0.1 N NaOH	24 hours	37	Colorimetric
	1	2	0.1 N HCl	24 hours	37	Ultra-centrif
	2	6.4	Ascitic fluid	8 days	37	Ultra-centrif
Bull quartz	2	9.1	Ascitic fluid	8 days	37	Colorimetric
Rock crystal	1	4.5	Pleural fluid	10 days	37	Colorimetric
Flint	1	24	Water	3 hours	100	Colorimetric
	1	43	1 per cent $NaHCO_3$	47 hours	37	Colorimetric
	1	18	0.1 N NaOH	27 hours	37	Colorimetric
	0.3	2.7	0.1 N HCl	24 hours	37	Ultra-centrif
	2	6.5	Ascitic fluid	8 days	37	Colorimetric
Granite	3	5	1 per cent $NaHCO_3$	48 hours	37	Colorimetric
Felspar	1	3.4	Water	3 hours	100	Colorimetric
Orthoclase	1	1.3	Water	7 days	37	Colorimetric
	1	0.8	0.9 per cent NaCl	7 days	37	Colorimetric
	2	0.8	Ascitic fluid	8 days	37	Ultra-centrif
Sericite	1	2.2	Water	3 hours	100	Colorimetric
	0.01	0.05	Water	2 months	37	Ultra filtr
	0.01	1	Serum	2 months	37	Ultra filtr
	0.1	0.8	1 per cent $NaHCO_3$	8 days	37	Colorimetric
	2	0.8	Ascitic fluid	8 days	37	Ultra-centrif
	0.1	0.4	1 per cent $NaHCO_3$	4 hours	100	Colorimetric
Mica	1	0.7	Water	14 days	37	Colorimetric
	1	0.45	1 per cent $NaHCO_3$	14 days	37	Colorimetric
	2	1.8	Ascitic fluid	16 days	37	Colorimetric
Asbestos	1	25	Water	3 hours	100	Colorimetric
	2	1.6	Ascitic fluid	8 days	37	Ultra-centrif
Fuller's earth	2	1.4	Ascitic acid	8 days	37	Ultra-centrif
Kaolin	2	0.4	Ascitic fluid	8 days	37	Ultra-centrif
		0.3	Ascitic fluid	16 days	37	Colorimetric
Talc	2	0.8	Ascitic fluid	8 days	37	Ultra-centrif

* The figures in this column give the amount of solid phase extracted with 100 ml of solvent

(1) King, E J, and McGeorge, M *Biochem. J*, 32, 417, 1938 (2) Fallon, J T., and Banting, F G *Canad Med Assoc. J*, 33, 404, 1935 (3) Archer, H E, quoted by Kettle *J Path and Bact*, 35, 395, 1932 (4) Lucas, C C., and Dolan, M *Canad Med Assoc J*, 38, 1938 (5) Briscoe, H V A, Matthews, J W, Holt, P F, and Sanderson, P M *Bull Instn Min Metall Lond*, April and June, 1937 (6) Titus, A C. *J industr Hyg*, 19, 138, 1937 (7) Myers, W M *U S Bur Mines Rep. Invest.*, No 2548, 1923. (8) Treadwell, F. P, and Hall, W T *Analytical Chemistry*, 8th ed, 1932 New York, J Wiley & Sons (9) King, E J *Nature, Lond*, 140, 320, 1937.

(From King and Belt · *Physiological Reviews*, 18, 329, 1938)

tinued for a number of days, after which period saturation would normally be assumed, the concentration of the dissolved silicic acid depends upon the mass of the silica extracted and the size of the particles. The initial phase of the dissolution of silica, when there is a high rate of solution, is also demonstrable indirectly; a rapid increase in the conductivity of pure water is observed on adding powdered silica.[80]

The high initial rate of solution of quartz has been attributed to the presence of surface imperfections and to a disturbance of the surface caused by abrasion,[33, 34, 81] the surface being likened to the Beilby layer found on polished metals. However, no evidence of a disturbed layer could be found in electron diffraction photographs[35] of silica surfaces, and it is difficult to reconcile the fact that the abnormal solubility phenomena are shown by powdered fused silica with a theory which postulates organized and disorganized layers

The initial rapid dissolution was also attributed to trace impurities, such as alkali metals,[79] and to rapid solution from sharp corners and protruding edges.[82] These theories are improbable, however, because powders may still show the unusual solubility characteristics after being repeatedly extracted with water, and some samples used for the solubility determinations contained insufficient small particles to account for the mass which dissolved rapidly.

There is evidence[32] that the anomalous solubility characteristics of silica are due to an incomplete monolayer of adsorbed silicic acid on the silica surface The evidence for this layer is as follows·

(1) When silica is extracted with alkali and the solute concentration is plotted against time, the part of the curve which corresponds to the slow reaction shows a linear concentration-time relationship. Extrapolation of this part of the curve until it cuts the axis at zero time (Fig. 5 2, curve A) indicates the amount of silica (e g. 0·13 mg /g on a powder of surface area 1 m ^{2}/g) which dissolves rapidly. As a monolayer, this amount would extend over 0·16 of the surface of the powder

(2) Silica powder which has been treated in this way with alkali, if washed, dried and re-extracted with alkali, dissolves more slowly than the original (Fig. 5.2, curve B), and it will rapidly adsorb from

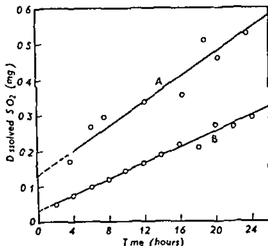


Fig 5 2 Rate of d ssolution of silica powder in 0 1 N—sodium hydroxide

Curve A or g nal powder curve B alkal -extracted powder

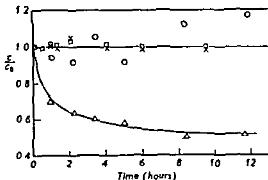


Fig 5 3 Change in the total s licic acid and rad o active s l cic acid concentrat ons in labelled s l cic acid solution to which quartz powder was added

(C_0 = n t al concentra on C = concentrat on after the t me n licated
rad a t c a l c a d pH 9
to al s l c c a d pH 9
rad o a t e s lic c a d pH 5
total s licic a d pH 5)

(F gs 5 and 5 3 are from Holt and K ng J chem Soc 1955 p 273)

a silicic acid solution an amount of silicic acid equivalent to that rapidly removed by the alkali.

(3) Silica in the layer, but not silica in the lattice, will exchange in alkaline but not in acid solutions with a silicate solution labelled with silicon-31 When a silica powder is added to a "saturated" ^{31}Si-silicic acid solution at pH 5, neither the total concentration of the silicic acid nor the concentration of the labelled silicic acid in the solution is changed (see Fig 5.3). If the experiment is carried out at pH 9, the total concentration of the silicic acid is still unaltered, but the concentration of the labelled silicic acid is reduced, indicating that exchange has occurred between the dissolved silicic acid and the silicic acid that is adsorbed on the silica surface

It is possible to check these observations by making similar calculations on the published results of other workers. In a number of these, both the curves representing the rate of solution of silica powders and the particle diameters were given or could be deduced. If it is assumed that the fraction of the surface covered by the silicic acid monolayer was the same in all the dusts, it is possible to calculate the specific surface of the dust from the mass of silica which dissolved rapidly These values may be converted into average particle

TABLE 5 2

Author*	Particle diameter (μ)	
	Observed	Calculated from hydrated layer theory
1	1–3	1
2	1–3	0·25
3	5–7	2 6
	0 5–3	0 3
4	2–5	2
	0 02–0 06	0 02
5	0 2–0 5	0·13
	0 33	0 13
	0 27	0 09
	0 27	0 06
	0 25	0 03
6	50–200	95

* (1) Briscoe, H V A, Holt, P F, and Sanderson, P M *Trans Inst Min and Metall*, 46, 291, 1936–37 (2) King, E J, and McGeorge, M *Biochem J*, 32, 417, 1938 (3) Lucas, C C, and Dolan, M *Canad Med Assoc J*, 40, 127, 1939 (4) King, E J *Occup Med*, 4, 26, 1947 (5) Kitto, P. H, and Patterson, H S *J Industr Hyg*, 24, 59, 1942 (6) Clelland, D W, Cumming, W M, and Ritchie, P D *J App Chem*, 2, 31, 1952.

diameters by assuming that the surface area-particle diameter relation is the same in all the powders and measuring this relation for a silica powder The observed and calculated diameters are set out in Table 5 2 The divergence between the calculated and the observed values increases as the particle size decreases, probably due to uncertainty in the optical estimation of the diameter of very small particles According to the calculated results, these samples must have contained particles which were below the limit of resolution of the optical microscope

Effect of pH and temperature on the solubility of silica

The solubility of silica varies but little with pH below pH 9 Above pH 9 the solubility increases rapidly with pH (Fig 5 4) The solubility increases with increase in temperature (Fig 5 5)

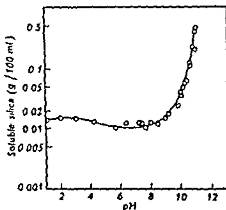


Fig 5 4 *Solubility of silica variation with pH (see Alexander, Heston and Iler, J phys Chem* 58, 453 1954)

Meaning of the comparative solubility values

It is useful to interpret the earlier "solubility values" in the light of the result
silica We
in two stages
first dissolv
second process is a very slow one and if the mass of the adsorbed silicic acid is insufficient to saturate the solution, no equilibrium

a silicic acid solution an amount of silicic acid equivalent to that rapidly removed by the alkali.

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4	2–5	2
	0 02–0 06	0 02
5	0 2–0 5	0 13
	0 33	0 13
	0 27	0 09
	0 27	0 06
	0 25	0 03
6	50–200	95

* (1) Briscoe, H V A, Holt, P. F, and Sanderson, P M *Trans Inst Min and Metall*, 46, 291, 1936–37 (2) King, E J, and McGeorge, M *Biochem J*, 32, 417, 1938. (3) Lucas, C C, and Dolan, M *Canad Med Assoc. J*, 40, 127 1939. (4) King, E J *Occup Med*, 4, 26, 1947 (5) Kitto, P. H, and Patterson, H S *J Industr Hyg*, 24, 59, 1942 (6) Clelland, D. W, Cumming, W M, and Ritchie, P D *J App Chem*, 2, 31, 1952

Dissolution of mineral silicates

When silicate minerals dissolve in water or when silica dissolves in the presence of metal ions the systems are far more complicated and no adequate study of them has been made Certain features are apparent however A silicate mineral will not pass into solution as

TABLE 5 3

Dissolution of Quartz in 0 05 N Na_2CO_3
Variation of dissolved SiO_2 with weight of quartz extracted

Wt of quartz (g) extracted by 100 ml 0 05 N Na_2CO_3	Wt of SiO_2 (mg) in 100 ml of solution
1 0	0 27
2 0	0 48
3 0	0 66
4 5	1 08

The quartz powder was extracted for 4 days at 18 C (Briscoe H V A Matthews J W Holt P F and Sanderson P M *Trans Inst Min & Metall* 46 291 1936–7)

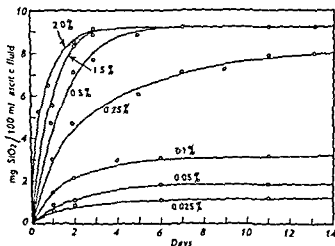


Fig 5 6 Dissolution of quartz (rock crystal powder) in ascitic fluid at different ratios of solid to solute (King and McGeorge *Biochem J* 32 417 1938)

between the solid and the solute will be established until a very long time—perhaps several years—has elapsed. If the total surface of the extracted dust is large (the mass of the dust is large relative to the mass of solvent and the particle size is small) then equilibrium is established and the solubility is the same as the absolute solubility of silica gel as determined by Lenher and Merrill[78] and Alexander, Heston and Iler.[52]

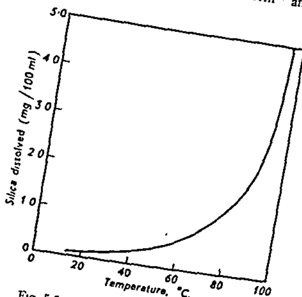


Fig 5 5. Dissolution of quartz in water.

The curve shows the variation with temperature of the mass of the dissolved silica after 4 hr when 1 g quartz (particle size mainly 1–3 μ) was extracted with 100 ml water (Briscoe, Holt, Matthews and Sanderson *Trans Instn Min Metall*, 46, 291, 1936–37)

Most of the solubility determinations which have been made of silica by extracting the silica for an arbitrary time—hours or days—will have measured mainly the extent of the adsorbed layer of silicic acid So far the results of the investigations appear to show that the adsorbed layer covers approximately the same proportion of the surface of every sample of pure silica. The solubility values previously published will, then, be a measure of the surface area of the dust samples, and consequently it would be expected that the "solubility" of quartz as it has usually been determined will vary with the amount of dust extracted This is, of course, exactly what has been observed, for example, by King (Fig. 5 6), and by Briscoe and others (Table 5 3). This reasoning will apply to any pure silica dust.

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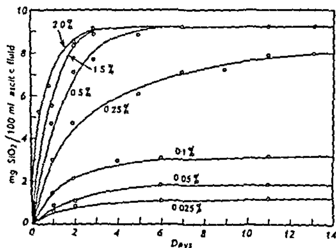


Fig 5 6 Dissolution of quartz (rock crystal powder) in ascitic fluid at different ratios of solid to solute (King and McGeorge *Biochem J* 32 417 1938)

such. The lattice consists of orderly-packed ions and the water will have a leaching action, removing more soluble oxides and leaving the less soluble. This means that the mineral particles may eventually become coated with an insoluble film of metallic hydroxides, which will prevent further dissolution.

When a silicic acid solution contains also ions of a polyvalent metal it usually happens that a precipitate forms slowly. These precipitates have often been observed but have not been investigated; they are most probably salts or complexes of the metal with polysilicic acid. If these precipitates are formed, the concentration of silicic acid in the solution will be reduced and the apparent "silica-solubility" of the mineral will be low. The observed values for the "solubility" of silicate minerals, such as shale, and of impure forms of silica such as sandstone are much smaller than that of pure silica. Moreover King[84] has observed that when sandstone and shale are extracted with water the concentration of the dissolved silica at first increases with time but then decreases (Table 5.4). Similarly Whitehouse,

TABLE 5.4

Solubility of Sandstone and Shale in Water

Time, months	Solute concentration (mg. SiO_2/100 ml.)	
	Sandstone	Shale
1	1·26	4·07
5	2·04	3·09
10	1·87	1·05
15	1·12	0·34
20	0·80	0·27

(King, E. J. *Occup. Med.* 4, 26, 1947.)

extracting mineral silicates with dilute sodium carbonate, found that the concentration of silica in the solution increased during the first 48 hours but, in most cases, it decreased thereafter.

When the metal ion that passes into solution with the silica is sodium or potassium, insoluble silicates are not formed and the solubility may appear higher than that of pure silica. It seems likely that monovalent cations will appear to increase the silica solubility, and that polyvalent cations will appear to decrease it.

The formation of the precipitates which we have assumed to be metal polysilicates requires only a small amount of the metal ion. It is apparent then that traces of metal impurities in samples which

are used for solubility determinations will considerably alter the silica solubility values. How important is the effect of metal ions on the fibrogenic activity of silica is not known.

Since the introduction of the Solubility Theory of Silicosis the effects of many substances on the concentration of dissolved silica in water silica dust systems have been studied. Many substances have been found to depress the solubility of quartz. These include metals such as iron and aluminium and the corresponding metallic oxides and silicate mineral such as shale and mica. This effect again is probably due to the formation of metallic polysilicates at the surface of the quartz or the precipitation of polysilicates from the solution.

CHAPTER 6

THE INTERACTION OF SILICIC ACID WITH TISSUE COMPONENTS

More than half a century ago silicon was reported as a constituent of normal tissues. As early as 1897 Drechsel and Winogradow described the extraction of siliceous material from goose feathers They believed the substance was an orthosilicate of the formula $Si(OC_{34}H_{59}O)_4$ and an ester of an alcohol related to cholesterol. Isaacs[85] inferred the presence of silicolipins in brain. Holzapfel,[86, 87] investigating the composition of lung tissue in silico-tuberculosis, found organosilicates, "compounds in which the free valencies of the silica framework, instead of being satisfied with inorganic elements, such as calcium and magnesium, are satisfied with organic radicals". She further reported both nitrogen-free and nitrogenous organic silicon compounds as derivates of carbohydrates and proteins, and assumed that compounds similar to the phosphatides exist in which one or more phosphorus atoms are replaced by silicon. Holzapfel suggested that silicon also occurred in combination with glycerol esters Ohlmeyer and Olpp[88] assumed that esters of silicic acid are present in the tissues. A positively charged silico-carbohydrate complex was demonstrated in gelatin, ox tendon, horse and ox blood and human urine by electrodialysis [89] But although silicon has been reported as occurring in so many different types of organic compounds in biological material, there is no case recorded in which a compound has been isolated

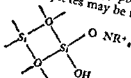
Silicic acid whether in the form of the monomer or of a polymer is a very weak acid The molecule will, then, possess far more unionized than ionized hydroxyl groups. There are two ways in which silicic acid may combine with other molecules. It may form salts by combination with a positive ion or it may become attached by the formation of hydrogen bonds between the hydroxyl groups of the silicic acid and hydroxyl or other groups of another compound. Both types of interaction are known.

The interaction of silicic acid with simple ions and with polar substances

Salts of silicic acid with organic bases have been prepared in crystalline form. In these compounds the acid and base are present

in stoichiometric proportions. Presumably silicic acid will react with many other organic bases although it is not always easy to prepare such salts in solid form

If the silicic acid is polymerized, it can still combine with bases The salt will then consist of a macro-molecule of silicic acid in which a few of the charges on the outside of the particle are neutralized by organic cations If, for simplicity, polysilicic acid is given a condensed structure, the complexes may be represented thus

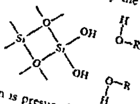


Since the combination involves electrovalent links, there will be ready interchange between the organic cations and any other cations which may be present in the solution

Combination occurs also between silicic acid and highly polar structures, for example, lecithin The resulting micelle will have an internal, negatively charged silicate structure surrounded by a positively charged layer of adsorbed organic ions, this layer is again surrounded by a negative, diffuse "gegenion" layer The solubility of these complexes in organic solvents will depend on the proportion of (hydrophilic) hydroxyl groups of the silicic acid polymer which are blocked by the (hydrophobic) organic residues

Interaction between silicic acid and simple non-ionic organic substances

Silicic acid is a weak acid and the majority of the OH groups will be undissociated The hydroxyl groups can become linked with the hydroxyl groups of other substances by the formation of hydrogen bonds, thus



This type of interaction is presumably involved in the formation of complexes of silicic acid and, for example, cholesterol It is probably the formation of these complexes which affects the polymerization rate in silicic acid solutions when substances such as glycol are present

In the case of polysilicic acids or even silica surfaces, the products will have the form of adsorption complexes. The two interacting substances will not combine in stoichiometric proportions. The interaction is usually demonstrated by some change in the physical properties of the silicic acid. For example, when added to aqueous solutions of certain substances which occur in tissues such as cholesterol or lecithin, silicic acid can be extracted by organic solvents such as alcohol or dioxan in which it is normally insoluble.[90]

In the tissues, the formation of complexes may be expected between silicic acids and many of the soluble biological substances which have a strongly polar group or a group which can combine with a hydroxyl group by hydrogen-bond formation. The multiplicity of the types of organic compounds which have been reported to occur in the tissues can then be readily understood. It seems doubtful whether any reaction of silicic acid with the organic molecules of the tissues occurs in stoichiometric proportions, and there is no evidence that silicon takes part in any biosynthetic process. It seems likely that, when the silicic acid has formed a complex, it will be unable to produce tissue damage because the outer surface of the micelle consists of organic groups which effectively isolate the silicic acid—an unusual type of detoxication.

Ionic interaction between silicic acid and proteins

Method of study.—Proteins are polyelectrolytes. They have the form

—CO CHR.NH.CO.CHR.NH—

in which R is an amino acid side chain which sometimes contains a charged group.

Silicic acid, both in the simple and in the polymerized state, is ionized and consequently it will react with polyelectrolytes and, in particular, with the charged proteins in tissues. When silicic acid reacts with simpler molecules, the interaction can sometimes be studied by isolating a crystalline product or by studying the effect of a second substance on the solubility of the silicic acid in organic solvents. These methods are often inapplicable to the study of the interaction of silicic acid with macromolecules, although similar methods may occasionally be used.

The interaction of silicic acid with proteins has been investigated mainly by studying the effect of the silicic acid on protein monolayers. The protein is spread on the surface of a liquid, usually a salt solution, so that it forms a layer which is one molecule thick. The layer is compressed and the force of compression (surface pressure) and the area occupied by the film are measured. From graphs in which the area is plotted against the force, the characteristics of the film may be

deduced Small molecules or ions may be attached to the film without any great effect on the compressibility of the film but adsorbed macromolecules interfere with one another when a film is compressed, and then the force/area curve is altered

From the point of view of the silicosis problem, the protein films which are of most direct interest are those of collagen A silicotic nodule is an orderly mass of collagen fibres and the formation of the nodule has probably been induced by silicic acid formed by the dissolution of dust particles The study of the interaction of silicic acid with collagen and its precursors is, then, a necessary part of any research on the formation of nodules Mainly because of its insolubility, collagen is a difficult protein to use in the form of a monolayer Since other proteins react with silicic acid it is often useful to study more amenable proteins than collagen and from their behaviour to deduce the probable behaviour of collagen The properties of some protein films will be described

Albumin —If an albumin film is compressed, the force/area curve has the form shown in Fig 6 1, curve A [95] With increasing pressure the area of the film at first decreases rapidly as the widely separated protein units are collected together (I) Once they are brought into close proximity, further increases in pressure on the closely packed units cause only small decreases in the area occupied by the film, the force/area curve rises steeply (II) At still higher pressures the arrangement of the protein molecules changes and an increase in pressure now produces a greater diminution in area (III), until at a critical pressure the film crumples

When unpolymerized silicic acid is present in the solution beneath the film, the form of the force area curve is unaltered This does not necessarily mean that there is no interaction It means that any interaction which has taken place has not altered the properties of the film Simple silicate ions will be freely exchanged with any other anions which may be present in the subsolution, so no alteration in [illegible]

between the units of the two species and the protein chains will form a less compact layer when the film is compressed This explains why the film shows a great resistance to compression and why the force/area curve is steeper If the adsorbed silicic acid polymerizes, the film becomes rigid This secondary polymerization, which considerably alters the properties of a protein, occurs at about

pH 6 to 6·5 Silicic acid can be shown to react with films of most proteins, but their properties are altered only if the silicic acid polymerizes The manner in which protein chains may be locked together by polysilicic acid is illustrated by the photographs of molecular models (Fig. 6.2).

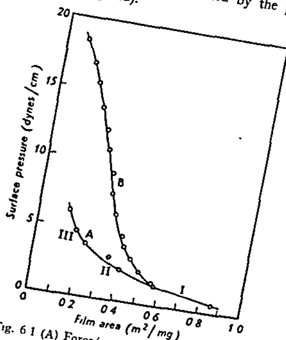
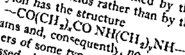


Fig. 6 1 (A) Force/area curve of an albumin monolayer on salt solution
(B) Polysilicic acid in the substrate makes the film much less compressible

At first (I) there is a rapid reduction in the film area with increased pressure The film then becomes less compressible (II) until (above III) it crumples and breaks down

Nylon.—Interaction between the protein and the silicic acid likely to be by electrostatic attraction between the ionized silicic aci and positively charged side-chains of the protein in the first place A second type of interaction is possible by hydrogen bond formation between the unionized hydroxyl groups of the silicic acid and the hydroxyl or amino groups of the protein. When the reaction of a protein with silicic acid is studied by the monolayer technique, it is difficult to differentiate between interaction due to attraction between ions and that due to hydrogen bond formation. Some information on this point has been obtained by studying the interaction of silicic acid with nylon films.

Nylon has a skeletal structure which resembles that of a protein, it differs in that the chain has been formed by the condensation of diamines with dicarboxylic acids rather than by the condensation of amino acids. Nylon has the structure



$$-CO(CH_2)_xCO\,NH(CH_2)_yNH-$$

It has no side chains and, consequently, no ionized groups.

When monolayers of some types of nylon are spread on salt solutions and compressed, the force area curves which they give closely resemble those given by protein films 90. If polysilicic acid is added to the substrates the properties of the films are altered. The films occupy larger areas, they are less compressible and they are stable at high pressures. This shows that interaction takes place between silicic acid and nylon, as nylon is not a polyelectrolyte, the interaction can occur only because hydrogen bonds are formed. Since the backbone of the nylon molecule resembles that of a protein, it seems certain that proteins also can react with silicic acid by hydrogen bond formation. When a polysilicic acid particle is attached by hydrogen bonds to a protein the bonds are not likely to be readily broken, the complex will be relatively stable and unaffected by small changes in ionic concentrations.

Collagen.—It is difficult to study collagen monolayers and consequently they have not been examined in such detail as those of some other proteins. Mature collagen is insoluble in all the usual solvents. Gelatin is a degraded collagen which is very soluble in water but it has properties different from those of native collagen. 'Hide powder' is an extracted collagen which more nearly resembles gelatin than native collagen (Chapter 7). A fraction of native tendon collagen can be dissolved in 0 1 per cent acetic acid and this solution gives satisfactory monolayers.

Collagen monolayers are much more compressible than are those of albumin 91, probably because the hydroxyproline and proline groups permit the molecules to fold in a way that albumin molecules cannot. The type of folding is illustrated in the photographs of the molecular models in Fig 6 3. When the collagen monolayers react with polymerized silicic acid, their compressibility is much reduced. Moreover, if after a first compression the pressure is reduced to zero and then the film is again compressed, the film shows an even lower compressibility. This is illustrated in Fig 6 4 which shows the effect of polysilicic acid on a collagen film at pH 7 2, i e, close to the pH of the body.

Silicic acid will convert most protein films to rigid layers at pH 6 to 6 5, the pH at which the silicic acid polymerizes further beneath the film. Collagen films are made rigid over a much wider pH range, approximately pH 3 to 9. When the film is compressed, the

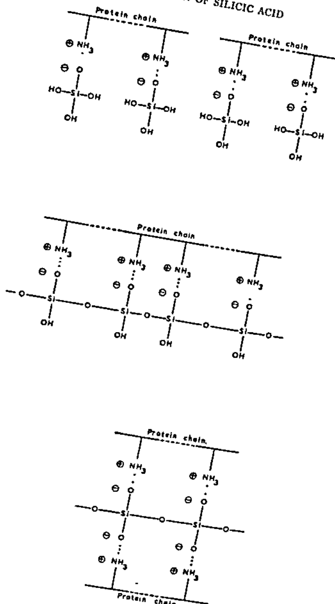
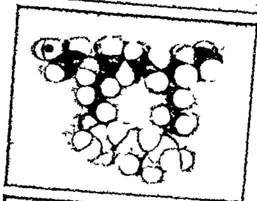


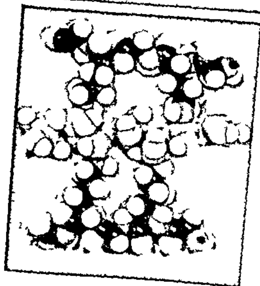
Fig 6 2 Model illustrating (A) the combination of a protein chain with orthosilicic acid molecules, (B) the "locking" of a protein chain by the polymerization of the silicic acid, and (C) the parallel binding of two protein chains by polymerized silicic acid.



(A)



(B)



(C)

reactive parts of the chains are probably brought into close proximity and they are tied together by the polysilicic acid. Possibly, the conversion of procollagen into collagen is an analogous process.

It is apparent that, at the pH of the tissues, silicic acid and collagen interact. If the silicic acid were sufficiently concentrated, the properties of the collagen (or rather, the collagen precursor, because that is what is actually spread as a monolayer) would be drastically altered. In a later chapter it will be argued that this interaction may be responsible for the conversion of collagen precursors into collagen fibres in the formation of silicotic tissue.

When silicic acid reacts with a protein in bulk solution, the form of



Fig 6.3 Molecular model showing the folding of a polypeptide chain in which there are proline and hydroxyproline residues.

the product depends on the size of the silicic acid particles. If the silicic acid is present in the form of large polymers, the protein becomes adsorbed to the surface of the polymers. If the silicic acid polymers are small the silicic acid becomes adsorbed to the surface of the protein. Thus, Liberti and Benedetti[100] produced artificial collagen fibres, visible in the electron microscope, from collagen solutions and silicic acid of low molecular weight. Only amorphous precipitates were formed when the silicic acid had a high molecular weight (Chapter 7).

Adsorption of proteins on quartz

Silica particles will adsorb proteins from solution. Between pH 3 and 10, the amount of albumin which is adsorbed on to quartz increases with the pH value[102]. The mass of protein which is adsorbed from a 0·25 per cent albumin solution by quartz is four times greater at pH 3 than at pH 7·4. The amount adsorbed varies

with the concentration of the albumin solution, at pH 6·8, 15 mg are adsorbed on to 10 mg quartz of particle size 1–3 μ from a 0·01 per cent solution and 125 mg from a 5 per cent solution. Similar results are obtained with bovine albumin, fibrinogen and rabbit serum. The character of the protein as judged by antibody reactions

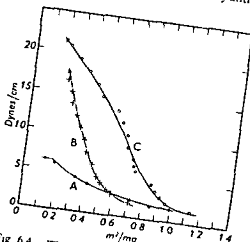


Fig. 6.4. The effect of silicic acid on the force/area curve of a collagen monolayer. ● Substrate free from silicic acid. ○ 0·002 M silicic acid. + 0·0005 M silicic acid. Curve B approximates to curve A until the protein film is reduced to an area of 0·6 m²/mg. When the film is compressed further curve B lies nearly parallel to curve C. This shows that when the concentration of adsorbed silicic acid reaches a critical value polymerization takes place and the properties of the protein are altered. (Clark, Ph.D. Thesis, University of Reading)

is changed by the adsorption process. It has been suggested that the initiation of fibrogenesis in silicosis is due to the adsorption and alteration of tissue proteins on the surface of the inhaled quartz particles (Chapter 11). The adsorption of substances (presumably proteins) from serum on to quartz has also been shown by electron microscopic studies.[101]

CHAPTER 7

FIBROUS TISSUE

Connective tissue

The connective tissues of the body[93] consist of cells embedded in intercellular substance. The connective tissues proper always have fibres present in the intercellular (ground) substance and several types of tissue are differentiated according as one or other type of fibre is prevalent. elastic tissue has an abundance of elastic (yellow) fibres, fibrous tissue contains mainly collagen (white) fibres. Areolar tissue, the loose irregular connective tissue which attaches the skin to underlying structures and fills spaces between the organs, contains both elastic and collagen fibres.

The intercellular substance is predominant in cartilage although fibres are still present, and consequently cartilage is the tissue usually used as a starting material for the isolation of the ground substance Cartilage consists almost entirely of the sclero-protein collagen, chondroitin sulphuric acid and perhaps other acidic polysaccharides. When viewed under the optical microscope cartilage appears to consist of isolated cells separated by a ground substance which is apparently homogeneous Digestion with trypsin or the use of a silver impregnation technique shows that the ground substance is not homogeneous but contains a network of collagenous fibrils, sometimes running in all directions, sometimes gathered into orientated bundles.

The general structure of all connective tissue is that of a coarse network of collagen bundles the meshes of which are filled with a ground substance of fine reticulin fibres associated with polysaccharides of high molecular weight (mucopolysaccharides; associated with protein they form the glycoproteins) One function of the ground substance is that of storing and transporting water and electrolytes

Permeability of connective tissue

This structure of connective tissue has been confirmed by measuring its permeability by recording the rate of flow of saline through the fascia from the skin of a mouse. The interfibrillary

substance upon which the permeability must be largely dependent is thought to consist mainly of protein,[103 104 105] but the flow through the tissue is increased some ten or twenty times by the enzyme hyaluronidase which hydrolyzes glucoproteins.[106, 107 108] If hyaluronidase-treated tissue is perfused with starch or dextran solution, the flow is reduced again and remains reduced when the starch solution is replaced by saline.[109] Removal of the starch with an amylase again increases the permeability (Fig 7 1)

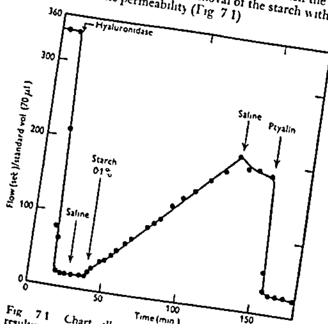


Fig 7 1 Chart illustrating the increased permeability resulting from treatment of a membrane of fibrous tissue with hyaluronidase

Permeability is reduced by starch but it increases again when the starch is removed by ptyalin (Day T D J Physiol 117 1 1952)

The effect on the rate of flow is determined not only by the concentration of the perfusing dextran solution, but also by the molecular weight of the particular dextran used (Fig 7 2) Other macromolecules, agar, chondroitin sulphate gum arabic and pectin, and diluted serum produce similar effects to those shown by dextran and starch.[110] Silicic acid has been shown similarly to reduce the permeability of hyaluronidase treated membranes[111] Its effectiveness depends on its degree of polymerization (Fig 7.3)

The cellular components of connective tissue which are revealed by histological methods could not offer the resistance to the flow of saline which is shown by the membrane of mouse connective tissue, since these components are separated by spaces of up to 50 μ diameter. A protein component of the interfibrillary spaces is believed

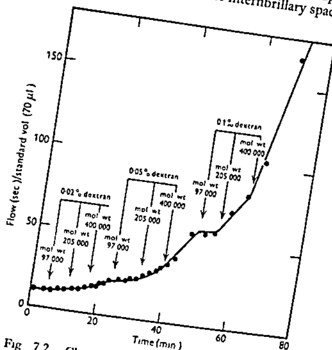


Fig 7 2 Chart showing the reduction in the permeability of a hyaluronidase-treated membrane produced by dextran.

The degree of reduction depends on the molecular weight of the dextran (Day, T D, *J Physiol*, 117, 1, 1952)

to act as a sieve capable of retaining macromolecules. Normally the meshwork is filled by molecules or molecular aggregates of polysaccharides, such as chondroitin sulphuric acid or hyaluronic acid, but it is evident that other macromolecules could behave similarly. It has been suggested that chemical forces do not come into play in the interaction of the macromolecules with the protein meshwork, but the only macromolecules used in this experimental work have a carbohydrate structure and the formation of hydrogen bonds between the hydroxyl groups and proteins cannot be ruled out.

Production of natural collagen fibres

The cells ...
fil ...
fib ...
als ... proliferate ... formed unless ... be secreted by fibroblasts[118, 119] or perhaps by mast cells

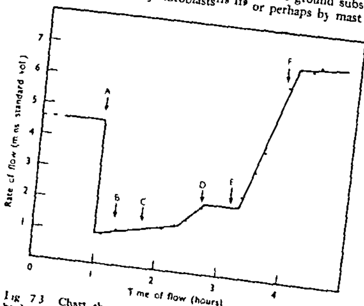


Fig 7 3 Chart showing the reduction in the permeability of a hyaluronidase treated membrane produced by polysilicic acid (Holt P F and Osborne S G *Brit J Industr Med* 10 152 1952) A = hyaluronidase B = saline C = fresh silica sol 0·2% D = saline E = silica sol 0·2% aged 2 hours F = saline

from a heparin like precursor[120] In very ... blasts and also of osteobl... m ...

... fibres ... elements may ... up to 500 Å long ... although ... be the precursors of collagen It has been

Fibres have been produced in tissue cultures In cultures of rat thymus the fibres were always found to appear near to cells As early as 1929 Maximow[122] believed they were precipitates formed from soluble substances in the medium Initially the fibres stain

like reticulin (see below) but after 25–30 days they become re-orientated and then stain like collagen Doljansky and Roulet[123] maintained a tissue culture on one side of a porous glass filter and grew fibres, which stained like collagen, on the other. They also believed that the fibres were produced outside the cell. Porter[124] suggested that a gel layer just beneath the cell membrane may be organized into collagen fibrils or that a gel may be exuded and polymerized into fibres at the cell surface.

Reticulin

In many specimens of connective tissue two collagen-like structures have been differentiated mainly by staining reactions. The true collagen is stained yellow-brown by certain silver impregnation techniques (e g Maresch-Bielschowasky) whilst a similar ... reticulin, is stained black Collagen fi... lin fibres branch and anastomose
very fine network of reticulin fibr
immature[152] collagen ...
than is collagen
such as the silver
polysaccharide

Collagen is stai... but reticulin is not stained by the fuchsin of van Gieson's picro-fuchsin stain. Collagen is but slightly affected by the periodic acid-Schiff test but reticulin stains red The periodic acid-Schiff reaction probably colours both the protein and the carbohydrate moieties of the collagen Periodic acid reacts to produce aldehydes with compounds containing two adjacent unsubstituted hydroxyl groups or one hydroxyl group adjacent to a primary or secondary amino group. Polysaccharide sulphates are stained metachromatically by thionin and toluidine blue.[125] According to Meyer[126] these dyes demonstrate mainly the chondroitin sulphate in the tissues. They also stain quartz metachromatically.[27]

Electron micrographs appear to show that reticulin has a membranous structure[127] Minute randomly orientated collagen-type fibrils are embedded in a structureless matrix which is probably a glucoprotein Collagen is in the form of definite fibres and the transition of reticulin to collagen appears to involve the aggregation and orientation of the reticulin fibrils into bundles, accompanied by a reduction in the amount of structureless mat... connective tissues of ... l
reticulin. In ...
bundles of fibrils ... this tissue, no
... In sections of other tissues there is a continuous series of structures, randomly orientated fibrils, thin

fibres and thick fibres. The fibrils are soluble and the ground substance is insoluble in boiling water.

A lipid component of reticulin probably containing a myristic acid group has been described[128].

The effects of ascorbic acid and cortisone on fibrogenesis

Ascorbic acid and cortisone are known to affect the metabolism of collagen. Ascorbic acid is not essential for the maintenance of preformed collagen[129, 130]. Experimentally the formation of large amounts of collagen can be induced by injecting subcutaneously into animals an extract of Irish moss. If the animals are fed on a diet deficient in ascorbic acid Irish moss extract produces very little collagen[131]. Wolbach and Howe[132] some twenty five years ago suggested that ascorbic acid is necessary for the gelation of an intracellular fluid matrix secreted by fibroblasts. The abnormal swollen collagen fibres which are produced when the diet lacks ascorbic acid are embedded in a large amount of matrix[133, 134].

Under some conditions cortisone appears to inhibit the formation of connective tissue. It is not certain how the effects are brought about. The macrophages may be affected[135] or the fibroblasts may be selectively injured[136]. It may have a direct effect on the fibroblasts or the matrix in which the cells develop[130] or it may inhibit chondroitin sulphuric acid formation[131, 132]. Cultures of lung embryo in embryo extract produce large amounts of collagen. Cortisone does not decrease the rate of formation of this collagen unless the culture is produced from a cortisone treated embryo[136]. Other studies[137] seem to suggest that cortisone has no effect on the production of collagen *in vivo*.

Any influence of cortisone on the production of collagen fibres may be due to an effect on the production of acid mucopolysaccharides. This has been studied but the results are somewhat confusing. Layton[138] for example reported that cortisone inhibits the synthesis *in vitro* of chondroitin sulphate in embryonic and wound tissue but Schiller[139] observed no effect on the production of mucopolysaccharides in the combs of chicks. Curran[97] found that the total amount of mucopolysaccharide in quartz induced lesions of the lung was reduced by cortisone but that there was no complete inhibition.

The structure of the fibres

Electron microscopic studies of collagenous material separated from tendon, cutis and skeletal cartilage show that the fibrous structures which are seen in the optical microscope and which

normally make up a coarse network are composed *of fibrils, a few* hundred to a few thousand ångströms wide.[140, 141, 142, 143, 144, 145] A fine closely woven net of fibrils fills the spaces between the coarse *fibres.*

solitary structures and as very loose bundles. The fibres and fibrils seem to be of indefinite length. Similar fibrils and protofibrils have been produced in tissue cultures.[147]

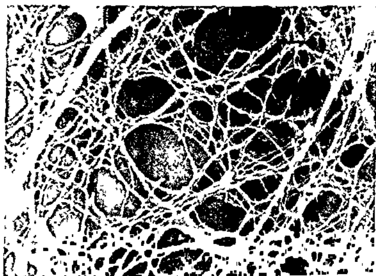


Fig 7 4 Electron micrograph of membrane of fibrous tissue which shows protofibrils, fibrils and fibres (Day and Eaves, *Biochim. et Biophys Acta,* 10, 203, 1953.)

These structural arrangements are considered to be characteristic of connective tissue generally
exists between fibres, fibrils,
Assuming that a polypeptide
dimensions of the cross section are 11·5 and 4·4 Å[148], the cross sectional area of a chain is $5\times10^{-7}\ \mu^2$. About two thousand molecules then make up a fibril of 0·05 μ diagonal length (i e. area of $10^{-3}\ \mu^2$). Fibrils are extensible, they can be stretched considerably beyond their normal length.

PROPERTIES OF COLLAGEN

Amino acid residues of collagen

Collagen, the water insoluble structural protein of connective tissue, has a minimum molecular weight of 39 000 in solution. Its composition differs from most other body proteins in that it has a high content of hydroxyproline (present in small amounts in elastin also but absent from most other animal proteins), proline and glycine residues. Hydroxylysine is also present in collagen but in no other animal protein except elastin. Cystine, cysteine and tryptophane residues are absent and tyrosine and methionine occur only in very small amounts (Table 7.1). Thirty eight per cent of the amino

TABLE 7.1

Amino acid Residues of Albumin, Gelatin and Collagen

Bowes, J. H. and Kenton, R. H., *Biochem. J.* 43, 359, 1948, and Stein, W. H. and Moore, S., *J. Biol. Chem.* 178, 79, 1949

	Albumin	Gelatin	Collagen
Glycine	1.6	26.9	27.2
Alanine	—	9.3	9.5
Valine	7.7	3.3	3.4
Leucine	11.0	5.23	5.6
Isoleucine	1.7		
Proline	5.1	14.80	15.1
Phenylalanine	7.8	2.55	2.5
Cysteine	0.7	—	
Half cystine	5.6	—	—
Methionine	1.3	0.9	0.8
Tryptophane	0.2	—	—
Arginine	6.2	8.55	8.59
Histidine	3.5	0.73	0.74
Lysine	12.3	4.60	4.47
Aspartic acid	10.4	5.6	6.3
Glutamic acid	17.4	11.2	11.3
Serine	3.7	3.18	3.37
Threonine	5.0	2.20	2.28
Tyrosine	4.7	1.0	1.0
Hydroxyproline	—	14.5	14.0
Hydroxylysine	—	1.2	1.2

acid residues are polar (contrast 3 per cent for elastin) and the number of free basic groups is almost equal to the number of free acidic groups. The isoelectric point of the collagen of beef tendon is

7·0 There is more glutamic acid and hydroxyproline and less tyrosine and proline in the collagen of rat skin than in the collagen of the tail.[149]

The amino acid residues in collagen are arranged in a highly specific order The sequence is thought to be[164, 184]:

glycine—any residue except proline or hydroxyproline —any residue, but usually proline or hydroxyproline

No terminal amino groups have been detected.[150] This might be explained either by assuming that the molecule has a cyclic structure or that the molecular weight is so high (several million) that the methods of detection are insufficiently sensitive. It has also been suggested that the terminal end-groups may be aspartic acid residues which are masked by mucopolysaccharides or other groups

End-groups have been detected in procollagen and in collagen which has been heat-treated or treated with urea, hyaluronidase or formic acid.[150] The order of abundance of the different terminal groups in modified collagen is as follows: aspartic acid, glutamic acid, glycine, alanine and threonine. With the possible exception of aspartic acid, these end-groups are considered to be produced by the hydrolysis of peptide bonds during treatment.

The amino acid residues in collagen may be investigated by a [illegible]

[illegible] amino acids are separated by paper chromatography. [illegible] collagen may be estimated by measuring the hydroxyproline content of the [illegible]

amino

gelatin

indicated a marked similarity. Their chromatograms resembled those given by collagen derived from several other sources

Dissolution and chemical fractionation of collagen

Collagen swells, then partially dissolves in dilute mineral and organic acids. Collagen (e g. hide powder) also dissolves in anhydrous formic acid, and a method of extracting collagen from the tissues with hot trichloracetic acid has recently been described[153] About 30 per cent of the collagen in the tendon of a rat's tail is soluble in 8×10^{-3} M acetic acid[154] and, similarly, the collagen of other tissues can be separated into acid-soluble (collagen A) and insoluble (collagen B) fractions.[155, 156] The amount of acid-soluble

collagen decreases as the tissues age[154] The skin collagen of growing rabbits has been fractionated[157] into material soluble in phosphate buffer pH 9, material insoluble at pH 9 but soluble in citrate buffer pH 3 8, and an insoluble residue Only a part of this insoluble

Degradation of collagen to gelatin: Stability

The prolonged heating of collagen with water results in the dis-

such as keratin, are absent from collagen In collagen cross-

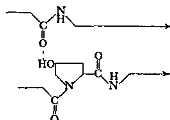
perature at which this reduction in length occurs ("shrinkage temperature") is altered when the collagen is pretreated with certain reagents

The part played by the mucopolysaccharides in stabilizing the

reduced to about 53° and its solubility in acetic acid is greatly increased

The shrinkage temperature of collagen depends on its source

Gustavson[163] found that N-acetylated collagen had a shrinkage temperature which was approximately the same as that of the collagen from which it was prepared. If the collagen was both N- and O-acetylated, the shrinkage temperature was lowered from 64–66°C to 40–44°C. He deduced that interchain cross-links are ruptured by O-acetylation. By the methods used, all the amino groups could be acetylated and 80 per cent of the hydroxyl groups Gustavson stated that his findings are in conformity with the cross-linking of protein chains by the hydroxyl groups of the hydroxyproline to keto-imide groups, thus:



Effect of silicic acid on collagen stability—When collagen (rat-tail tendon) is treated with hyaluronidase its shrinkage temperature is reduced The shrinkage temperature is restored to normal when the tendon is treated with silicic acid (Table 7 2).[195] Saline slightly raises the shrinkage temperature

TABLE 7.2

Observed Shrinkage Temperatures of Rat-tail Tendon following indicated Treatments

Condition of tendon	Shrinkage temperature °C*	
	After soaking in water	After soaking in saline
Native	65	67
Hyaluronidase-treated	56	62
Silicic acid treated (following hyaluronidase treatment)	64	67

* Each value is a mean of at least six determinations

Photomicrographs of a piece of teased tendon are illustrated in Fig 7 5 In saline and in water the native tendon is opaque After treatment with hyaluronidase the tendon still appears opaque when placed in saline, but it becomes swollen and transparent in water (A) This change is reversible, the tissue contracting laterally and appearing opaque when returned to saline, but resuming its swollen condition in water

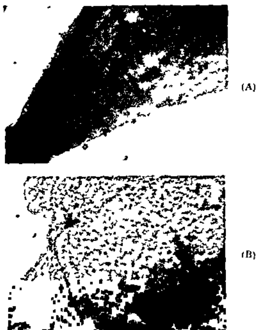


Fig 7 5 Splayed end of a piece of rat tail tendon in water (A) after treatment with hyaluronidase (B) after treatment with hyaluronidase, then silicic acid

When the

bonds Electron microscop·
that collagen fibres consist c
chains packed together, wit
matching transversely.[166] The molecule may consist of a single polypeptide chain, or possibly[167,168] three polypeptide chains joined to one another by hydrogen bonds, and each coiled into a helix Observations on the light-scattering properties of collagen solutions also suggest the shape of a long thread-like macro-molecule of about 12 Å diameter and are consistent with the model of a three-chain helix which was given by Pauling.[168] The total length is 150,000 Å but the thread is highly coiled

Metabolism of collagen

The earlier investigations on the amino acid turnover of collagen in connective tissue indicated a constant anabolism rather than constant destruction and formation to produce the equilibrium state which has been demonstrated in some other tissues.[169,170] The rate of formation of new collagen in normal tissues is very low but it is high in healing wounds and in developing tissue. Studies made at the National Institute for Medical Research[171,172] indicate that if a growing rat is fed ^{14}C-labelled glycine, the glycine becomes rapidly incorporated in its collagen. The collagen is, in fact, constantly being broken down and replaced but this process is slow compared with the catabolism of other proteins.

Studies with radioactive glycine[157] suggest that the alkali-soluble collagen is a precursor of the insoluble collagen B When α-^{14}C-glycine is fed to rabbits, it becomes rapidly incorporated in the "alkali-soluble" fraction of the skin collagen, at a rate comparable ... proteins, after reaching
from this fraction
...n" increases and
The radioactivity ...
decreases much more slowly and the increase and decrease in the insoluble fraction is even less marked

Reconstituted collagen fibres

On adding certain salts to a solution of collagen, a fibrous precipitate is formed.[173] These reconstituted fibres resemble native collagen in their staining reactions but their properties depend to some extent on the acid used as solvent.' ... (tendon) solutions

in acetic acid give a fibrous precipitate with 10 per cent sodium chloride solution If 1 2 per cent acetic acid ... original solution the ... fibres being refor...
0 4 per...
chlo...
pitat...
chlo...
which are reconstituted...
acid are almost insoluble in 0 4 per cent acetic acid ... chondroitin sulphuric

Microscopic observation of a fibre dissolving in sodium chloride solution has shown that just before solution is completed the material is a mass of tapered rod like structures 2 5 μ long which sometimes show end to end aggregation Shaken with 2 per cent aqueous sodium chloride the fibres first split longitudinally with weaker sodium chloride solutions the filaments break up into short rods

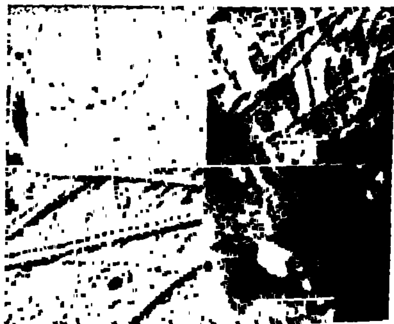
Both native collagen fibres and these reconstituted fibres show a typical banded structure when shadowed with uranium and viewed in the electron microscope The cross striations are spaced at intervals of about 640 Å [175] This corresponds to the repeat pattern shown by X rays [176] These bands are probably an indication of the molecular forces which bind the fibrils together

The fine structure of ... the conditions of repr... at 640 Å and 210 Å ... more than 2 000 Å and segmented fibrils [177] ... longer spacings at ... According to Vanamee and Porter[178] collagen (rat tail tendon) when reconstituted from a solution in 0 01 per cent acetic acid by 1 per cent saline at pH 4 8 6 8 first gives small fibres having striations every 210 Å Larger fibres are then formed which show striations at 640 Å Higher or lower saline concentrations produce long fibrils without striations higher pH values produce long slender fibres

The ground substance

Collagen is invariably even in white connective tissue associated in the tissues with the acid polysaccharides chondroitin sulphuric acid [179] first isolated in 1861 [180] and hyaluronic acid Both polysaccharides contain uronic acid residues Dried cartilage contains some 40 per cent of chondroitin sulphuric acid 100 g of fresh tissue from the human skin contains 26 mg chondroitin sulphuric acid and 24 mg hyaluronic acid [181] Rat tail tendon contains about one per cent of polysaccharide The polysaccharide content of skin is not completely accounted for by chondroitin sulphuric acid and hyaluronic acid [182] Other polysaccharides are present which can be

separated either by chromatography or electrophoresis on filter paper The ratio of collagen to chondroitin sulphuric acid is low in cartilage, which is normally subject to considerable tension[183]; it is higher in the cartilage of osteoarthritics than in healthy cartilage.[184] As cartilage ages its content of chondroitin sulphuric acid is reduced and, parallel with this reduction, there is a loss of elasticity.



F[illegible]

1 [illegible]
2 [illegible]
3 [illegible]
4 [illegible]

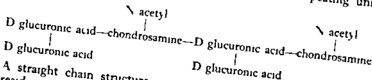
Marked changes in the nature of the ground substance, induced by heparin, hydrocortisone, deoxycorticosterone, hyaluronidase, etc., have been observed with the electron microscope (Fig. 7 6) The changes are thought to be due to alteration in the degree of polymerization of the ground substance. An increase in the fibrous elements induced by heparin may be caused by the precipitation of the "procollagen" which pre-exists in the intercellular matrix

Chondroitin sulphuric acid

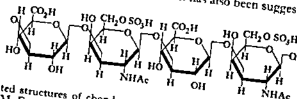
The glycoproteins are depolymerized by enzymes of the mucinase class, such as hyaluronidase and the physical state of the ground substance, which varies reversibly from that of a fluid to that of a rigid gel depends on the relative rates of format... zation of the glycoprote...
best extractec ... i-
Prepared in t ... s
this is reduce ... ,000–50 000 if even small ... of about 260 000 but alkali are used in the extraction process In the extracts chondroitin sulphuric acid is associated with protein and this glycoprotein is called "mucoid Its function appears to be that of f... links between collagen fibre... comb...
th... t
ior...

and polysaccharide[183 186] ... for carboxylic acid residues in both protein likewise ...

The ... elastin is worke...
hydrol... chondroitin sulphate ... has been deduced ... d is not ... On acid sulphuric acid D glucuronic acid shown by synthesis[187] to be glucopyranose 6 carboxylic acid and N-acetylchondrosamine[188 189] Chondrosamine is 2 amino 2 deoxy D galactose its constitution having been confirmed by synthesis A suggested structure for chondroitin sulphate[190] has a branched chain the repeating unit being



A straight chain structure containing about 120 monosaccharide residues connected by β linkages which has also been suggested[191] is



Suggested structures of chondroitin sulphuric acid (Meyer K H Odier M E and Siegrist A D *Helv chim Acta* 31 1400 1948)

Chondroitin sulphuric acid and other carbohydrates such as heparin and hyaluronic acid will precipitate certain proteins at acid pH,[192, 193] very long crystalline particles being formed in some cases Although a large concentration of chondroitin sulphuric acid is required, the amount carried down by the precipitate is very small It has been suggested[194] that this may represent the mechanism by which collagen fibres are formed in cartilage and in connective tissue, the chondroitin sulphuric acid cementing together the protein molecules to form fibres and, later, bundles.

Partridge[185] was the first to suggest that the role of chondroitin sulphuric acid was the orientation of collagen in developing connective tissue The fibres in healing wounds, arising from fibroblasts which invade the area, may become orientated into fibre bundles in a similar way In the clotting of fibrinogen also, rod-like fibrinogen molecules become longitudinally arranged into strands, and fibres are assembled by the parallel alignment of fibrils.[196]

Meyer[197] proposed the following theory of fibrillogenesis, although admittedly without proof Fibroblasts secrete large amounts of acid mucopolysaccharides together with a globular native protein, the precollagen The protein is precipitated and denatured on to the polysaccharide fibrils by acid, formed locally by the cells, and thus are formed the fibrous proteins of the reticulum. The regularly spaced acidic groups of the polysaccharide form the template on which the fibrous proteins are built up. Later, the polysaccharide is removed by enzymes

The nature of the links between collagen chains and between collagen and mucoproteins or chondroitin sulphuric acid was studied by Jackson[198] who used the two reagents β-naphthalene sulphonic acid which will eliminate salt-like cross links[199] and calcium chloride which affects hydrogen bonds.[200] He estimated that between collagen molecules the ratio of salt links to hydrogen bonds was 9·40 and between chondroitin sulphuric acid and collagen 13·[illegible] and Hall[174] believe that chond[illegible] the end-to-[illegible]
the [illegible] n
and [illegible]
of te[illegible]

Hyal[illegible] acid

Meyer and Rapport[201] have reviewed the properties of hyaluronic acid It exists in the skin but in higher concentration in the vitreous and aqueous humors of the eye and in the umbilical cord[160] Cells appear to be cemented together by gels formed from this acid. Its "molecular weight" is believed to be at least 200,000–500,000

Solutions of the material extracted from these sources have high viscosities but they are lower than those of the fluids from which the acid is extracted This is undoubtedly due in part to the depolymerization of the polysaccharide on extraction but it may also be that the hyaluronic acid is associated with proteins in the native fluids

The acid is polydispersed both in native fluids and in extracts The aggregation of the polymers is believed to be due to weak secondary bonds Similar bonds may join the acid polysaccharide to proteins but they are broken when the acid is isolated

Solutions of the acid as normally prepared show streaming double refraction of flow Solutions of a hyaluronate show elastic recoil[202] because the long flexible ions form a lace work throughout the solution and are bound to one another and eventually to the walls of the containing vessels by hydrogen bonding When such solutions flow the hyaluronate ions are less mobile than the associated metal ions and the latter move in advance of the former An electrical potential is thus established and has been measured

Analyses of hyaluronic acid show that hexosamine acetyl groups and uronic acid are present in equivalent quantities A structure has been suggested in which N acetylglucosamine and glucuronic acid

solution remains clear The polymer is estimated by this reaction

Hyaluronic acid is hydrolyzed by hyaluronidases Preparations from different sources produce different degrees of hydrolysis so it is probable that several different enzymes exist

Little is known of the function of the acid Meyer said that the hyaluronidase system has continued to receive more of the attention of investigators than has the metabolism of hyaluronic acid or its role in animal physiology and pathology

Other polysaccharidic acids

Because chondroitin sulphuric acid and hyaluronic acid can be extracted in relatively large amounts the former from cartilage and the latter from the cornea much more is known about these substances than about other polysaccharides which are associated with fibrous

present only in very small amounts if at all but other polysaccharides are present The structure of these other compounds is uncertain

they contain hexoses (mannose and galactose) and hexosamine (probably glucosamine)[201] but not uronic acid. The work of the Taplow laboratories[204, 205] suggests that a sulphated polysaccharide of this type may be predominant in the ground substance of most connective tissue and that it is associated with a tyrosine-rich, and probably leucine-rich protein. Abdominal subcutaneous connective tissue, for example, when extracted with N/5 potassium hydroxide at 0°C yields a solution which contains carbohydrate and protein. On mild hydrolysis the carbohydrates yield hexosamine, galactose and mannose, as shown by chromatography and ionophoresis on paper, but no uronic acid Acidic polysaccharides can be demonstrated, but none is identical with the chondroitin sulphuric acid of cartilage. A sulphated mucopolysaccharide which does not contain uronic acid but does contain N-acetyl glucosamine and galactose has also been found in bovine cornea.[208]

CHAPTER 8

PHYSIOLOGICAL AND PATHOLOGICAL EFFECTS OF ADMINISTERED SILICA IN TISSUES OTHER THAN THE LUNG

I EXCRETION OF SILICIC ACID

The effects of ingested silica

Silica is much more abundant in vegetable than in animal tissues Very little is known about the form in which it occurs in plants and it is probably not essential for plant growth [207, 208, 209] Silica is thus a normal constituent of the animal diet Most of the dietary silica passes through the digestive tract and appears in the faeces but a part enters the intestinal wall, presumably as simple silicic acids, and appears in the blood

Part of the absorbed silicic acid is retained in the tissues but most of it is removed from the blood by the kidneys The fate of dietary silica can be judged from the results of an experiment in which the addition of 0 1 per cent of an extremely fine silica powder to the diet of rats produced an accumulation in the tissues of 0 8 per cent of the amount ingested, 4 per cent appeared in the urine and 95 per cent in the faeces

The silicon which is retained in the tissues, is normally fairly evenly distributed over the body Published values for the tissue silicon of human and animal tissues are given in Table 8 1 The wide variation between the values of different observers is probably due to the peculiar difficulties which have been encountered in the estimation of silica in the presence of phosphate It is very desirable that further determinations should be made by the more accurate methods[210] which are now available After the administration of large amounts of silicic acid the silicon level in the kidney may be much higher and the level in the more vascular organs slightly higher than in the other tissues

The forms in which silicon exists in animal tissue have been investigated Organic compounds containing silicon have been reported [211, 212, 213] but it is more probable that the silicon is present as adsorption complexes of silicic acid with proteins and other polar

organic constituents of the tissues.[80] These complexes were described in Chapter 6.

The urinary excretion level of silica normally depends on the diet, consequently the normal values for carnivora are much lower than

TABLE 8 1

Silica Content of Animal Tissues

	SiO_2(mg./100g. tissue)	Reference*
ADULT TISSUES		
Blood ash (human)	1,500	7
Lung (human)	140	3
(rabbit)	170, 202	3
Liver (human)	6–8	2
(,,)	11–17	3
(rabbit)	200	3
(,,)	12–30	5
(ox)	12–22	5
Kidney (human)	2–7	2
(,,)	11–27	1
(rabbit)	7–12	2
(,,)	14–22	5
Spleen (human)	15–41	1
(,,)	17	6
(,,)	6	2
Muscle (human)	15–45	1
Bone (,,)	25, 26	5
Hair (rabbit)	15, 16	5
FOETAL TISSUES		
Blood (human)	13	5
Brain (,,)	22	4
Heart (,,)	20	4
Kidney (,,)	13	4
Liver (,,)	4–6	4
Lung (,,)	8–10	4
Muscle (calf)	24–37	4
Spleen (calf)	24–37	4

* 1 Belt, Irwin and King (1936) 2 Isaacs (1924) 3 King (1928) 4 King and Belt (1938) 5 King, Stantial and Dolan (1933) 6 Schulz (1901) 7. Böhme and Kraut (1932)

those for herbivora (Table 8 2) The values can be increased or decreased by changing the diet[214] or by adding to it soluble silicates or silica[101] Table 8 3 shows the effect on silica excretion of changing the diet of rabbits

TABLE 8 2

Silica Content of Urine

		SiO_2 mg /100 ml			SiO_2 mg /100 ml
NORMAL HUMAN				No	
Average of 10 morning samples		1 2 (extremes 0 8 2 1)	Rat (lab diet)	1	3 0
Average of 17 afternoon samples		1 0 (extremes 0 7 2 2)		2	5 7
SILICOTIC HUMANS (gold miners)			Cat	1	0 5
W L C		1 4		2	0 3
J I		6 6		3	0 5
J L		1 9 (1 week later)		4	0 8
J D		1 0		5	0 7
J M		0 6		6	0 4
ANIMALS			Rabbit	1	11 1
Dog	No			2	27 2
	1	0 9		3	22 7
	2	1 3		4	21 3
	3	1 8		5	7 2
	4	0 7		6	14 0
	5	1 3		7	15 6
	6	2 7	Guinea pig	1	14 0
				2	22 4
				3	28 6
				4	16 6
				5	14 6
				6	8 2
			Sheep	1	17 2
				2	12 8
				3	11 9

Experimentally silica has been administered to animals as soluble silicates or silicic acid and as mineral silicates As might be expected orally administered silicic acid produces a large increase in the urinary silica[215] A far greater increase is produced by the sol than by the gel[216]

Silicates which are readily decomposed by the hydrochloric acid in the stomach also produce a large increase in the silica excreted in the urine Magnesium trisilicate which is administered clinically in large doses may increase the excretion from about 1 to 50 70 mg[217] A smaller increase is also found after administering powdered

TABLE 8 3

Effect of Diet on Silica Content of Rabbit Urine

Rabbit No	.	232	233	234	235
Diet	Days on diet	mg SiO_2/100 urine			
Oats, carrots					
White bread	20	8 5	12 8	10 3	34 3
	7	3·6	2 5	2 1	4 0
	10	4 4	3 9	5 6	4 6
	15	0 9	2 8	1 4	2 2
	17	0 7	2 5	2 9	2 9
	22	4 1	2 6	—	3 1
	26	—	2·7	0 9	3 6
	32	5 5	2 2	1 5	0 7
Oats, wheat straw	1	15 1	27·2	25 7	19 3
	4	27 0	24 5	12 0	24 7

(Table 8 1–8 3 are from King, E J., Stantial, H , and Dolan M *Biochem J*, 27, 1002, 1933)

quartz,[215] flint, or the silicate mineral, Scotch whinstone.[216] The increased excretion in man following the ingestion of cement is represented graphically in Fig 8.1

Since the presence of some minerals in the alimentary tract will produce an increase in the urinary silicon level, it is difficult to prove whether inhaled dust trapped in the lung affects the urinary silicon values A large part of any inhaled dust is always coughed up and swallowed or transferred to the oesophagus by the cilia of the bronchi and so reaches the alimentary tract. Any increase in urinary silicon may either be due to dust in the alimentary tract or it may represent silicic acid which has entered the blood directly from the lungs It has been stated[218, 219] that workers who have been exposed to atmospheres in which the silica dust concentration is high, excrete more silicon than others even some years after they leave the industry The differences recorded are small, however, and may not be significant

In spite of the high silicic acid excretion rates which are known to occur in certain conditions, no pathological effects in man have been ascribed to a high silica diet. It has been reported[220, 221] that cataract in India is associated with a high silicon content of the lens, but a diet high in silica did not affect the eyes of rats. It is possible,

however that the renal calculi composed almost entirely of silica which are frequently found in sheep in Western Australia and the southern states of America may be the result of a diet high in silica and deficient in water combined with the effects of a hot dry climate

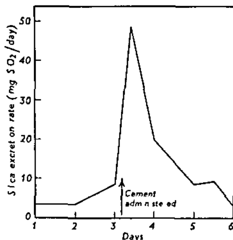


Fig 8 1 Increase in the silica content of the urine following the oral administration of cement (Holt *Brit J industr Med* 7 12 1950)

Injected silica

Sharp increases in silica excretion follow the injection of sodium silicate or silicic acid into animals Even powdered minerals when injected intraperitoneally into animals may give definite though smaller increases [222] indicating that the minerals are somewhat soluble in the tissue fluids (Table 8 4) Cement produces a large increase in urinary silicon when administered by intraperitoneal injection [223]

The blood concentration may be so high that polysilicic acid is formed the particles of which are too large to pass from the blood through the kidney glomeruli The amount of *silicic acid excreted*

TABLE 8.4

Increase in the silica content of the urine following the intraperitoneal injection of powdered minerals (King, E. J., and McGeorge, M., *Biochem J* **32**, 426, 1938)

	Av. excretion before administration	Excretion of silica (mg SiO_2) (hourly) 1	2	3	4	5	6	7
Amorphous silica	0·09							
Quartz (very fine)	0·07							
Flint (air-sedimented)	0·05							
Flint	0·08							
Felspar	0·08							
Sericite	0·09							
Whinstone	0·08							
Fuller's earth	0·08							
Daily:								
Quartz	1·6	4·3	2·7	2·8	2·2	2·9	2·3	—
Flint (air-sedimented)	1·2	4·6	4·1	4·1	2·0	1·6	1·9	—
Flint	0·9	3·5	1·9	1·1	1·1	1·0	—	—
Felspar	0·9	1·1	1·9	1·1	0·8	1·0	—	—
Whinstone	1·5	1·6	1·4	0·5	1·0	1·1	1·1	—
Fuller's earth	2·0	2·9	2·9	1·6	0·8	1·5	—	—



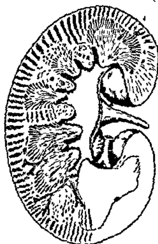


Fig 8.2 Autoradiograph of a section of a rat's kidney after the intraperitoneal injection of radioactive silicic acid, and diagrammatic section of kidney for comparison (Yates, Ph D. Thesis, University of Reading)

increases therefore, with increase in the amount of sodium silicate injected up to a certain value If more silicic acid is injected there is a decrease in the amount excreted The concentration of silicic acid in the kidneys of rats after the injection of various concentrations of silicate is shown in Fig 8 3 When injected intraperitoneally highly polymerized silicic acid is absorbed very slowly into the blood and the blood silica concentration never then reaches a high value

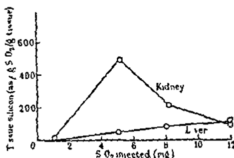


Fig 8 3 Liver and kidney silicon of a rat after injecting sodium silicate Variation with amount injected (Holt and Yates *Brit J exp Path* 35 52 1954)

II TISSUE RESPONSE TO INJECTED SILICIC ACID AND SILICEOUS MINERALS

When silicic acid or siliceous minerals are injected into animals the pathological effects which may be observed are of two types A rapid reaction of the organism may result in death after a few days or even hours or the material may slowly affect the tissue which responds by laying down dense fibrous tissue Any foreign body reaching the tissue may evoke a reaction which is initially inflammatory but finally results in the encapsulation of the foreign body by a thin deposit of fibrous tissue This is well known as a foreign body reaction The typical reaction which is initiated by some siliceous materials is one in which much denser layers of fibrous tissue are formed

(i) *Fibrogenesis*

Silicic acid

Silicic acid sols injected intravascularly may produce fibrotic

changes in the liver and kidney.[225] Rabbits injected daily with 10 mg. SiO_2 as a sol, and killed after 16 weeks had considerable fibrosis in the liver. Thick bands of fibrous tissue occurred immediately under the capsule, and finer tracts radiated from the intralobular veins and ran between the columns of liver cells. The kidney had lesions in the glomeruli and a thickened capsule. In some animals the tufts were also involved, but the tubules were generally unaffected. Similar, though less pronounced lesions

were undamaged but observed generalized degeneration of the tubular epithelium Knowledge of the exact site is important since

injected intraperitoneally cause fibrosis.[226, 227, 228, 229]

Silica and siliceous dusts

Types of tissue reaction provoked by dust.—Miller and Sayers[230] classified the types of reaction which may be elicited by injected dusts, with the object of establishing a test for dusts which are liable to cause fibrosis. By injecting saline suspensions of a number of dusts into the peritoneal cavity of guinea pigs three types of response were differentiated All dusts give an initial foreign body reaction with the formation of a nodule and more or less oedema Harmless dusts then either slowly disappear (absorption reaction) or remain in the tissues without inducing cellular proliferation (inert reaction) The fibrotic nodules induced by dusts which produce silicosis,

present

calcite,

limestone, precipitated calcium carbonate, ... one and Portland cement. Carborundum, ferric oxide, anthracite and bituminous coal are inert in reaction Quartz, flint and chat (76 per cent SiO_2 with 25 per cent as angular quartz fragments) produce a proliferation reaction, but clay and felspar do not.[231]

Tissue reaction to silica—The following description of the reaction of the tissues

Curran.[232, 27]

Within 15 mi

omental tissues and by the third or fourth day all of it is so fixed. By this time the initial acute inflammation has subsided. There are many small collections of quartz in the omentum and mesentery but most of the dust forms into a few larger spherical masses at these sites and also in the pelvic fat and on the abdominal wall. These masses enlarge during subsequent weeks.

During the inflammatory stage polymorphs and nuclear fragments are present in large numbers around each quartz mass. Some cells are seen throughout the mass during the first 24 hours but these rapidly disintegrate. When this initial reaction subsides the cells in the exudate around the mass are mainly mononuclear and some

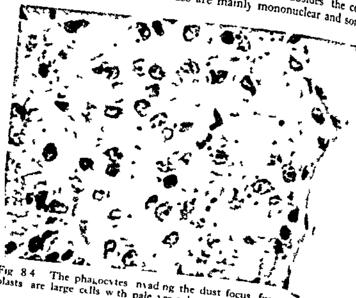


Fig 8 4 The phagocytes invading the dust focus. Fibroblasts are large cells with pale vesicular nuclei and abun[dant] laden cytoplasm

The small dark structures are nuclear fragments and dust partic[les] and en[...]n × 530)

invade the mass as macrophages and fibroblasts (Fig [...] reducing its size. It is some months before the large[r] are replaced by fibroblastic foci.

Reticulin forms in the dust masses very soon [...] there is a fine reticulin network in the smaller m[...] The network is first formed at the periphery of [...] reticulin is slowly replaced by collagen demonstrat[...]

Fig 8 5. Reticulin fibres are forming between the fibroblasts. (Gordon and Sweet's method. ×530)

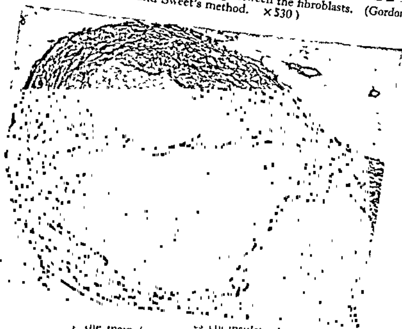


Fig
and
... encapsulate the quartz focus
... the main focus into smaller masses (Gordon and Sweet's method. ×65)

day (Fig 8 6) After several months the collagen takes the form of a typical silicotic nodule, which often has a whorled form

By staining reactions Curran[27] demonstrated that the fibroblasts in the quartz focus produce a mucopolysaccharide, possibly hyaluronic acid, before reticulin fibres can be demonstrated (Fig 8 7) A metachromatic staining reaction is given immediately the quartz is injected but this is due to the quartz itself and not to mucopolysaccharide

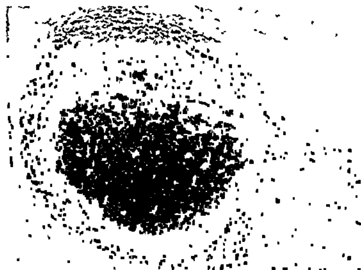


Fig 8 7 The focus is being invaded by fibroblasts which contain abundant mucopolysaccharide

This material released from the fibroblasts has impregnated the central mass of unphagocyted dust It is disappearing around the newly formed reticulin fibres (Hale's method × 65)

Figs 8 4 to 8 7 are from Curran *J Path and Bact* 66 271 1953

Tissue reaction to silica in different sites It has been repeatedly shown that powdered silica can produce fibrotic nodules in a number of sites in the body when injected into animals Gardner and Cummings produced silicotic lesions in the liver by injecting fine quartz powder intravenously Giese[231] injected rabbits with quartz The spleen liver and lymph glands of all the animals became fibrosed

Fig 8 5. Reticulin fibres are forming between the fibroblasts (Gordon and Sweet's method. ×530)

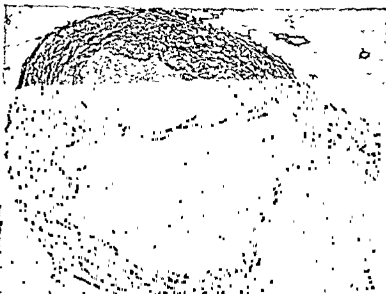


Fig 8 6 Young connective-tissue fibres encapsulate the quartz focus and others split up the main focus into smaller masses (Gordon and Sweet's method. ×65)

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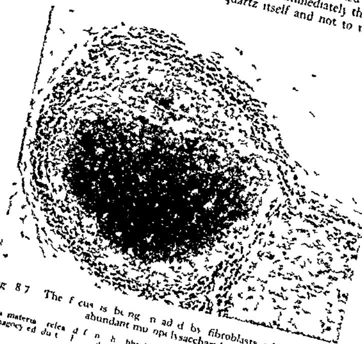


Fig 8 7 The f cus is be ng n ad d by fibroblasts h ch conta n abundant mu opolysaccharide

Th s materia relea d f n h fibrob a t has pregna d the en ral ma f unphagocy ed du t appea ng ar und he new f rmed re u n fib es Ha e h d ×65

F gs 8 4 t 8 7 are fr m C rran J P th B ct 66 271 1953

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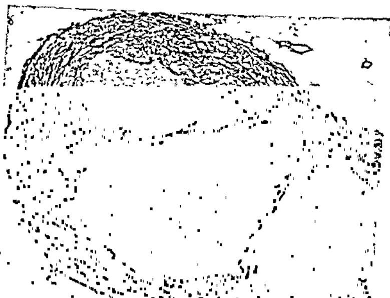
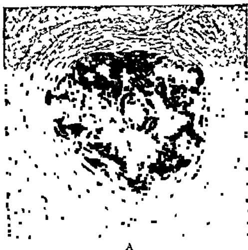
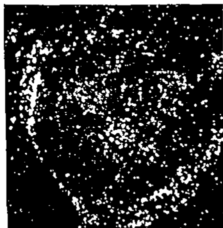


Fig 8 6 Young connective-tissue fibres encapsulate the quartz focus and others split up the main focus into smaller masses (Gordon and Sweet's method ×65)





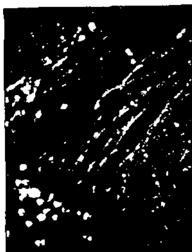


Fig 8.8 (A) Silicotic nodule in the human spleen. Reticulin Stain ×70. (B) Similar section showing HCl insoluble ash. At this magnification fine powdery ash in the centre of the nodule can be discerned. Dark field ×70. (C) Fine ash of nodule shown in B. It retains the outline of the fibres as though it had been incorporated into the tissue. Coarser silica particles are blurred at this magnification. Dark field ×240. (Belt, *J Path and Bact* 49, 39, 1939)

size range, injected into the ear vein of rabbits, are carried to the liver and in eighteen months the normal tissue is almost completely replaced by fibrous tissue Particles with a mean diameter of 1·7 μ produce a moderate amount of scarring; those with a mean diameter of 3 [illegible]
organ become[illegible]
to reach only [illegible]
spleen and the bone marrow [illegible]

The condensate which is produced when silica is fused, in which the silica particles are well below 0·1 μ in diameter, produces little or no fibrosis when injected into animals[240] but Policard and Collet[241] have produced fibrosis in rabbits by injecting silica of particle size below 0 15 μ intraperitoneally

The effect of cortisone on the action of quartz

The fibrogenesis normally induced when quartz powder is injected into the peritoneum of a mouse is suppressed by large doses of cortisone [242, 243, 244] The initial cellular response to the quartz may be normal but the fixation of the nodules is very much delayed [illegible] in the peritoneum
[illegible] ersed
[illegible] direct
effects on the individual phagocytes but the production of the cellular exudate which stimulates phagocytosis is inhibited In his experiments, even heavy doses of cortisone failed to delay the appearance of the first reticulin and collagen fibres.

The effects of cortisone on the tissue response to quartz are not observed in guinea-pigs and the retardation of fibrogenesis is less marked in the rat and the rabbit [242] Cortisone has no effect on established lesions caused by the intraperitoneal injection of quartz into rabbits but the production of further fibrosis around the lesion is retarded during the period of the administration of cortisone, diffuse connective tissue is laid down instead and there is vascular proliferation [245] A similar report was given by Curran on the effects of cortisone on established lesions in mice.

When quartz is injected into mice, the formation of nodules is not affected by injections of hyaluronidase, which hydrolyzes mucopolysaccharides It is thought unlikely, then, that the action of cortisone is due to a repression of mucopolysaccharide formation. Schiller[246] reports that the acute toxic effects produced by 20 Å silica are reduced by cortisone, and also[243] that some other hormones have an inhibitory and some an acceleratory effect on the formation of silicotic granulomas by quartz.

(ii) The rapid toxic effects of injected silica

Silica sols

Surprisingly little attention has been paid to the early effects of silicic acid sols and gels on animal tissues. The injection of as little as 1 ml of 5 per cent silicic acid (equivalent to 10 mg SiO_2 per ml) into the ear veins of rabbits may cause death within a few minutes, but death is probably due to embolism caused by floccules of silicic acid. On the other hand a dog has been injected with as much as 300 mg SiO_2 at a strength of 1 mg SiO_2 per ml over a period of 6 hours without causing death.

The main and most quoted work on the toxicity of silicic acid is that of Gye and Purdy[223] who injected both sols and gels into animals and observed toxic effects. Their sols were prepared by adding a dilute solution of sodium silicate to an excess of concentrated hydrochloric acid and dialyzing the resultant solution to free it from chlorides and sodium. Before injection the sols were filtered through a Berkfeld candle. On storage these sols polymerize, their viscosity increasing until a gel is formed.

The toxicity of these sols varied with the degree of polymerization of the silicic acid. When freshly prepared a 1 per cent sol injected intraperitoneally in 0.1 or 0.2 ml quantities immediately affected mice which died within 2 days, yet 0.3 ml of a similar sol which had been allowed to polymerize for 3 months had much less effect and killed only one mouse of six. Injected intravenously, a stored sol is more lethal than one which is freshly prepared. A lethal dose of a freshly prepared 1 per cent sol is approximately 100 mg per kilogram of body weight. A 3 per cent sol is more lethal. When the sol is given in one massive dose death occurs within one or two days but if smaller repeated doses are given the animal may survive much longer. Giese believed that silica had two effects, a toxic and a fibrogenic effect, the former being directly and the latter inversely proportional to the solubility of the specimen.

Recently Dale and King[247] have re-examined the acute toxicity of silicic acid. Using concentrations of only 5 mg SiO_2 per ml they found that doses of 1.2 mg would kill a 20 g mouse when administered intravenously. Particulate quartz (0.5–8 μ) had about one tenth of this toxicity, a value comparable with that of other materials such as aluminium hydroxide, India ink and corundum smoke. Dale and King suggesting that the toxicity is due to protein precipitation observed that silicic acid is only acutely toxic if the particles are of colloidal dimensions. Klosterkotter[248] found that molecularly dispersed silica was highly and rapidly toxic

The damage to tissues which Gye and Purdy produced with silicic acid sols has not been satisfactorily explained. When the experimental results are viewed in the light of modern knowledge of the properties of silicic acid, certain complicating factors are apparent

Most of the evidence for the toxicity of silicic acid is due to Gye and his collaborators; indeed, the conception of silicic acid as a tissue poison, which resulted in the development of the Solubility Theory of Silicosis, was a result of their work. Gye was careful to use pure silicic acid sols, which were prepared by dialyzing acidified sodium silicate until free from chloride He was careful to remove particulate matter by passing the sol through a Berkfeld candle before injecting it A salt-free sol at the concentration of one per cent, which he used, polymerizes very slowly. On the addition of sodium chloride, however, rapid polymerization ensues (Chapter 4). It is certain that, on dilution with physiological saline before injection or even on meeting the electrolytes of the blood, polymerization would be accelerated and the formation of floccules is possible. It is impossible to say whether the rapid toxic effects noticed by Gye were due, wholly or in part, to embolisms.

Gye and Purdy made a careful post-mortem examination of mice and rabbits which they had killed by the intravenous injection of a single dose of silica sol They found blood clots in the heart and the large venous trunks; when death occurred rapidly it was often due to intravascular clotting Animals repeatedly given smaller doses of silica sol usually survive for several days. At post-mortem they show petechial haemorrhages in the skin, gastric mucosa, heart muscle, lungs and elsewhere. The kidney is swollen. The glomerular tufts are enormously dilated. Serum and sometimes erythrocytes are in the capsular space. Sometimes the tuft is completely necrosed The tubular epithelium is much less affected although some fatty degeneration is present.

The liver shows focal necrosis; in some cases half the liver parenchyma is dead The liver cells may be represented by cell debris the columns of which are separated by dilated sinusoids packed with altered blood, or the cells may not be completely destroyed, pyknotic nuclei and vacuolated protoplasm remaining, and then the sinusoids contain but little blood. There is always considerable fatty degeneration Damage in the spleen may show either as a necrosis with disappearance of cells, those remaining being separated by a swollen reticulum, or an extreme congestion of the organism may be present in which case the blood sinuses are distended with blood.

Gye interpreted the rapid changes brought about by silicic acid sol as indicating that the primary action is on the vascular endothe-

lum He observed that a sol made isotonic by the addition of sodium chloride and injected into a rabbit considerably diminishes the clotting time of blood But the addition of silicic acid to blood *in vitro* does not affect its clotting time

Dust suspensions

Some dust suspensions have an immediate toxic action when injected 20 ångstrom silica a very fine powder formed as a sublimate in furnaces where silica is fused does not appear to cause silicosis nor does it produce fibrosis on injection If 50 mg of this silica in saline suspension is injected into the lungs of a rat or if 16 *mg* is injected intravenously it is highly lethal death results within a few hours sometimes almost immediately[84, 238] It is usually fatal if injected into the lung or the peritoneal cavity[248, 250] This silica sublimate *is* very soluble but according to King clear filtrates contain only about 15 *mg* silica per *100* ml solution a sol concentration far less than that of the silicic acid sols described earlier which caused rapid death in rabbits

The effect of the 20-ångstrom silica might be due to the particulate silica rather than to dissolved silicic acid however since very rapid death has also been observed following the intravenous injection of finely powdered quartz[251] Even finely powdered silica with a maximum particle size of 0 15 μ will invariably kill a rabbit when injected intravenously or intratracheally in a 30 50 mg dose[253] Death *may* occur immediately or within a few hours It is less toxic when administered intraperitoneally e g 100 mg doses killed only 20–30 per cent of a group of rabbits When injected into the lungs 20-ångstrom silica produces considerable oedema and congestion but no fibrosis

(iii) Bronchoconstrictor effects of silica sols

Colloidal silica will produce bronchoconstrictor effects when it is injected into the trachea of an anaesthetized guinea pig[252] or into the trachea of an excised guinea pig lung preparation[254] In the latter case fluid is fed at constant pressure into the trachea of a lung preparation and it leaves the lung through perforations made in the pleura The rate of flow of the fluid depends on the diameters of the smaller air vessels of the lung and constriction of these is shown by a reduction of flow Colloidal silica prepared by dialyzing an acidified solution of sodium silicate causes a definite constriction of the bronchioles when added to the perfusing fluid but soluble silica made by extracting quartz with water has no effect On the other hand particulate silica and aluminum hydroxide suspensions

system.

Klosterkotter[255] found that colloidal rather than molecularly-dispersed silica affected the contractile elements of the neurovascular system and led to a decrease in the blood-flow.

CHAPTER 9

DUST IN THE LUNG

Structure of the lung

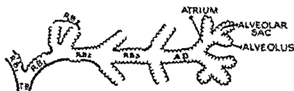




Fig 9.1 Respiratory air passages traced from the origin of a respiratory bronchiole to the alveolar duct

There is a mild degree of vesicular emphysema in this otherwise normal lung. Haematoxylin and eosin × 40. (Heppleston *J Path and Bact* 66 235 1953.) *TB* = terminal bronchiole (non-respiratory). RB_1, RB_2, RB_3 = respiratory bronchioles of the first, second and third orders respectively. *AD* = alveolar duct.

air-sacs, which are pushed out into minute bulges, the alveoli. The entrance to the air alveolus is known as an alveolar duct Muscle, elastic and reticulum fibres run obliquely round the alveolar duct,

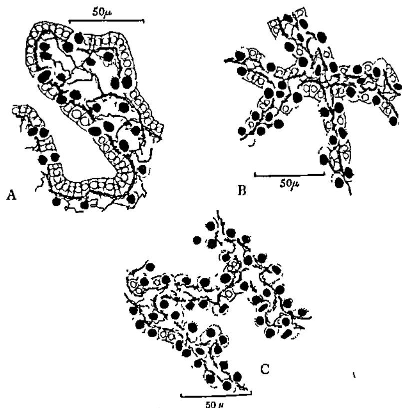


Fig 9 2 Alveolar epithelium in the human lung

but there is no muscle in the walls of the atria, the air sacs or the alveoli Excellent descriptions of the fine structure of the lung have been given [138,139] All but the smallest bronchi are lined by a columnar ciliated epithelium resting on a fine network of collagen

fibres, the basement membrane The lining of the smallest bronchi is non-ciliated and cubical

The alveoli —The layer of epithelial cells which lines most of the hollow organs of the body and usually lies on a basement membrane, is readily demonstrated by staining In early embryonic life, the developing lumen of the lung is lined in this manner by tall columnar epithelial cells supported by a reticular basement membrane But in the alveoli of the adult lung, neither epithelial cells nor basement membrane have been demonstrated[256], the surface structure presents an unsolved histological problem[257]

In the alveoli of the foetal rabbit lung a luminal epithelium is not found after the 26th day of the 32-day gestation period Before the 26th day the total volume of the epithelium increases but there appears to be no cell division in the distal parts of the lumen The inevitable cell rupture which follows is evidenced by the extrusion of degenerate cell nuclei into the respiratory lumen The basement membrane and the epithelial cells thus disappear as the development of the lung progresses (Fig 9 2) The epithelium of the more proximal parts of the lumen persists and the normal cell division occurs The distal parts become thus differentiated as the alveoli, and the proximal parts as the bronchioles After examining the alveolar walls in sections of adult lungs, Short[257] concluded "Nowhere was there an orderly nor numerous arrangement of nuclei to suggest the presence of a nucleated epithelium"

Blood supply — Branches of the pulmonary artery follow the bronchi and divide so that an arteriole accompanies each terminal bronchiole and leads to capillary networks surrounding the alveoli The capillaries approach closely to the lumen of the alveoli The capillary bed appears to be ensheathed by a delicate membrane containing reticular fibres which is continuous with the cytoplasm of the epithelial cells of the capillaries[257] In some places capillaries are in direct contact with epithelial cells of an alveolus, elsewhere a basement membrane may intervene

Lymphatic system — Lymphatics accompany the bronchi, the pulmonary artery and the pulmonary vein and they also occur as a network in the pleura, the membrane covering the lung There are numerous valves in the lymphatics of the pleura Lymphatics are absent from the walls of the atria and air sacs Lateral branches connect the lymphatics of the bronchi with those of the arteries and veins and these are often associated with patches of lymphoid tissue Aggregations of lymphoid tissue occur also at the divisions of the respiratory bronchioles[258, 259] All the lymphatics enter lymph glands at the root of the lung

A lymph gland is a mass of lymphoid tissue lymphocytes held in a

network of collagen fibres and contained in a fibrous capsule. The lymphocytes form rounded masses in the cortex of the gland but cord-like formations in the medulla. The lymphoid tissue is separated from the fibrous capsule by the lymph channel which is traversed by fibres, but in histological sections these fibres are largely concealed by masses of branched phagocytic cells which may contain dust particles transported in the lymph from the lung Lymph enters a gland by afferent lymphatics which lead into the lymph channel, it leaves by efferent vessels which originate in the medulla

The lymph glands at the root of the lung are a mass of small units. When inhaled dust has brought about pathological changes, new areas of lymphoid tissue, accumulation of lymphocytes traversed

this position

The fate of inhaled dust

Suspended dust may be removed from the inhaled air in the labyrinthine passages of the nose, or it may be deposited on the walls of the bronchi or bronchioles from whence it is swept back towards the oesophagus by the cilia. Nearly all the inhaled particles larger than 5 μ but very few particles less than 1 μ in diameter are retained in the nose.[262] Nasal efficiency varies considerably between individuals,[263] but amongst a group of sandblasters, nasal efficiency could not be correlated with susceptibility to silicosis.[264]

The alveoli of the lung always contain air (in man, the volume of the residual air is about 900 c c) and the exchange of gases in the alveoli is effected, ultimately, largely by diffusion It follows that only very small, light particles can reach the alveolar walls. A large proportion of the dust particles which enter the lung never comes into contact with the tissues; many particles remain suspended in the tidal air and are exhaled. Of the particles which are retained in the respiratory system, those between 0 2 and 1·5 μ are almost entirely deposited in the alveoli and the respiratory bronchioles [265]

Any process which will cause the fine dust particles in the air to

particles to aggregate and the aggregations that are inhaled are trapped mainly in the higher respiratory tract In tests on rabbits, which were placed in atmospheres containing silica dust, the aerosols considerably reduced the amount of dust reaching the lungs and, consequently, the degree of fibrosis induced

The relation between particle size and dust retention

The degree of retention in the alveoli of particles in different size ranges is shown in Fig 9 3 This curve was drawn by Davies[264] from data obtained by several methods and by a number of observers[262 267 268 269 270 271] Since different dusts were used in the several experiments, the values are corrected to apply to dusts of unit density There is maximum alveolar retention for particles of about 1–2 μ in diameter The suggested increase in the retention of particles in the smallest size range is based on very few observations

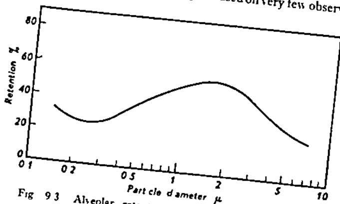


Fig 9 3 Alveolar retention of particles of unit density (Davies *Brit J industr Med* 9 120 1952)

In the range 0 3 2 μ, one factor which determines the degree of retention in the alveoli is the ratio of the volume of the tidal air to the respiratory rate[265] Van Wijk and Patterson[267] believe that Brownian movement is the main factor in the deposition of dust in the alveoli Hamilton and Walton[272] have suggested that the health hazard of a dust is better assessed by its settlement velocity than by the technique of sizing by means of the microscope

The size of the particles retained depends to some extent on their nature Bedford and Warner examined sections of the lung of a shot firer who died after working many years in an anthracite mine The size distribution of the dust in the lung was similar to that in the air of the mine Some of the particles in the lungs (0 3 0 4 per cent) were larger than 5 μ but all the larger particles were of coal and of the non coal particles 86 per cent were smaller than 0 8 μ[271] Practically all the dust particles found in a silicotic lung are less than 2 μ in diameter and most are less than 1 μ[273]

those found in the lungs is anything but good reasoning "

Phagocytosis

The dust particles which are deposited on the alveolar walls are engulfed by *scavenging white cells, the phagocytes* In sections of lung tissue, the phagocytes can be seen both attached to the alveolar wa
of
shc
from the alveolar lining [275] The normal cells of the alveoli may swell and become detached when dust makes contact with them, or there may be special and larger cells in the alveolar wall which function only as phagocytes

Some observers have not accepted this view. They have suggested that alveolar phagocytes are monocytes which have migrated from the capillaries[276] or that they originate in the bronchial epithelium [277] An observation made by Virchow[278] in 1858 is relevant. He noticed ... *ly free*

... lasmic processes are thrown out but are withdrawn under mechanical or electrical stimulus When a cell comes into contact with a foreign body, it tends to flow around the particle so that, if the body is small, it is drawn into the cell's cytoplasm. Using enzymes, the cell is able to destroy some foreign bodies; otherwise it moves with its load either outwards on to the epithelium of the bronchus where the cilia move the cell upwards until it is eventually coughed up, or possibly inwards via the lymphatics to the lymph glands [260]

A comparison has been made between leucocytes and macrophages when acting as phagocytes [279] Under the phase contrast microscope, *leucocytes in a tissue culture were seen to* move at a velocity of 25–30 μ per minute When the cell makes contact with a dust particle a projection from the cytoplasm (ectoplasm) surrounds the particle Small particles adhere in large quantities in the ectoplasm near the surface· they do not pass in quantity into the endoplasm If the particle is too large to be completely surrounded, the cell moves on, leaving part of the projection on the particle. Leucocytes do not take up particles larger than 3 μ.

... from the lung and spleen of chick embryo, move ... up to 10 μ in diameter ... lasm They show fatty



(A)



(B)

Fig. 14 Dust laden phagocytes

(A) Free cells packed w quartz part les x 1 800
(B) Quartz la n ell atta hed t the al eolar wall x 900   Few discrete d t particles are is ble in the yt plasm but the large n mber f particles a se d fract n f the l ght and re ul n a ottled appearan e

infiltration 3 days after taking up the dust and disintegrate on the fourth day.

The exact route to the lymph glands which is taken by phagocytes is doubtful. The phagocytes may carry the dust along the air-spaces to the nearest lymph vessels through which the dust is transported to the hilar glands[280]; they may carry the dust straight into the alveolar wall, then migrate along the tissue spaces into the perivascular and peribronchial lymphatics to the hilar glands[260]; or they

Fig. 9.5. Graphic representation of the increase in weight of lymph nodes of rats which received flint particles of different sizes, and in different amounts, to give a constant surface area of 700 cm², i.e., 199 mg of 4–8 μ, 100 mg of 2–4 μ, 42 mg of 1–2 μ, 18 mg of 0.5–1.0 μ and 8 mg of <0.5 μ. (Nagelschmidt, Nelson, King and Harrison, *Brit. J. industr. Med.* 11, 145, 1954.)

may migrate via the air-spaces to the vicinity of the lymphoid aggregations at the divisions of the respiratory bronchioles where they pass into the interstitial tissue and enter the lymphatic system[281]. Other possibilities are discussed on p. 109. The mononuclear cells which act as phagocytes when dusts are injected into tissues, also act as fibroblasts which are active in the production of reticulin fibres[27].

The readiness with which dust particles are engulfed by phagocytes may depend on the size and nature of the particles. Rat leucocytes in tissue cultures were found by Fenn[282] to take up quartz particles 4–5 μ in diameter more readily than particles 2–3 μ in diameter but

the observed differences only corresponded to the difference in the chance of collision between a cell and a particle Franks and Watt[283] found no such relationship between particle size and probability of phagocytosis, on the contrary they believed that the smaller silica particles were taken up more readily They observed that monocytes continued to take even fine particles (less than 0 5 μ) until they became turgid and rounded Selective phagocytosis of particles in the human lung has been demonstrated by studying the dust laden cells in the sputum [284] The median size of the intracellular particles was 1 15 μ The average size of the cells was 13 17 μ

The rate at which silica dust is transported from the alveoli to the lymph glands is determined largely by the particle size of the dust [285] at least when the dust is administered by intratracheal injection in one massive dose In King s laboratory flint dust in specified size ranges was administered to rats Two sets of experiments were run in one equal weights of dust were given to each animal in another each dose was calculated to have an equal surface area (700 cm ^{2}) In both sets of experiments the maximum amount of silica was found in the lymph glands after 12 months when particles of 1 2 μ diameter were injected there was less silica if the particle size was larger or smaller (Fig 9 5) When particles in the smallest size range (<0 5 μ) were administered a rapid increase in the silica content of the glands occurred during the first six months but there after the amount was almost constant The interpretation of these results is not easy since solution of the particles may occur both in the fluid of the lung and of the lymph glands

Large differences have been reported between the rates of phago cytosis of particles of different composition In tissue cultures manganese silicate particles were taken up twenty times less readily than manganese dioxide particles [286] Others[287] found no differential effects between quartz barium sulphate and coal in tissue cultures of spleen from chick embryo however

Gersing and Schumacher[288] found that carbon aluminium iron and limestone particles were taken up to about the same extent by macrophages in tissue cultures Quartz particles were phagocytosed more rapidly and the cells became vacuolated and lost activity sooner The quartz particles remained isolated in the cytoplasm although other dusts tended to agglomerate

It has often been suggested that readily phagocytosed dusts may stimulate the phagocytosis of other dusts particularly silica Using guinea pigs Carleton[275] found that coal dust which is readily phagocytosed caused the rapid elimination of simultaneously inhaled flint particles. Iszard[289] found that inhaled calcium hydrox ide dust stimulated the production of phagocytes in the lung and

retarded the development of disease in tubercle injected rabbits The suggestion has been made that there is an inverse relationship between the harmfulness of a dust and the distance it is phagocytosed from the alveoli in a given time [275, 290, 291]

The phagocytic cells are propelled by their own amoeboid movement, by the movement of the expired air and by the lymphatic flow.[292] In the network of tissue which supports the alveoli and the blood vessels of the lung, there are small collections of lymphocyte cells which tend to arrest and to trap the phagocytes. However, if the volume of the dust cells is greater than these traps can accommodate, the phagocytes pass by the lymphatic channels to the surface of the lung and then to the masses of lymphoid tissue in the glands at the root of the lung

TABLE 9.1

Silica Content of Peribronchial Lymph Nodes from 132 persons without History of Exposure to Siliceous Dust

Age group	No of cases in group	Percentage of SiO_2 in dry tissue (average)
stillborn	4	0 02
0 9	13	0 10
10–19	4	0 25
20–29	14	0 32
30–39	10	0 63
40–49	22	0 56
50–59	17	0 82
60–69	23	0 80
70–79	21	1 09
80–89	4	1 08

The masses of dust-laden phagocytes, both in the lung and in the lymph glands, become surrounded by a layer of fibrous tissue. The normal reaction of the tissues is to isolate any foreign body with a thin deposit of fibrous tissue. When the foreign body is silica, the fibrous capsule continues to increase until a nodule is produced which is so extensive as to be easily visible to the unaided eye

Silica in the lymph glands can be removed only by its dissolution in the lymph. If this process occurs at all, it is extremely slow Even in persons with no history of exposure to silica dust, the silica content of the peribronchial lymph nodes increases with age[293] (Table 9 1). In silicosis, if the exposure to dust is not prolonged or too intense, the protective processes function normally and for a long time there may be no functional indication of a silicotic condition.

As lesions become numerous a narrowing of the respiratory passages

the lung dust which has been administered by inhalation or by

wall they swell when in contact with dust then they become detached and carried away via the bronchi by the mucus flow Dusts which penetrate the connective tissue do so he believes without the aid of cells and the phagocytosis of these ducts occurs only after they penetrate the interalveolar walls

Dust deposits may be moved to the lymph glands without the intervention of phagocytes [296] As early as 1936 Akazaki[297] asserted that the dust particles moved in the lymphatics only in a free extra cellular manner It appears that the oedema fluid is the main agent in their transport Mottura[294, 95] found asbestos particles in the lymph nodes of a person who died from asbestosis which were more than twenty times as long as the diameter of a cell and he suggested that these must have been transported passively by the lymphatic flow Isolated extracellular quartz particles are often found in the interalveolar walls in silicotic patients and the dust in the lungs of coal miners which collects in the lymphoid tissue at the divisions of the respiratory bronchioles is observed in histological sections to be partly in the cytoplasm of phagocytes and partly free [281] The absence of any epithelium in the alveoli was emphasized earlier and Mottura believes that the fluid layer covering the alveolus is continuous with the interstitial fluid thus allowing the direct penetration of dust particles into the tissues

Macklin [298, 299] from a study of the lungs of albino mice concluded that alveolar phagocytes are normally fixed to the alveolar wall Very often they are detached from the wall by histological manipulations alveolar dust cells are readily dislodged from the alveolar walls merely by collapsing the lung In thousands of histological sections he found no unequivocal evidence of alveolar phagocytes entering the interstitium of the lung from the alveoli He believes that alveolar phagocytes can leave the alveoli only via the bronchial tree Dust laden cells in the connective tissues of the lungs have collected dust particles which have worked their way into the connective tissue *They are histocytes Superficially they resemble* alveolar phagocytes Other workers[300] support the views of Mottura and of Macklin

Hulse[649] suggested yet another mechanism. He believed that the phagocytes are normally present in the alveolar wall. They collect dust particles and may be dislodged, for example, by coughing If they are not dislodged, a growth of new epithelium may occur over the dust-laden cells, the new cells also being phagocytic. An accretion thus forms and the larger the accretion the less likely is it to [illegible] The cells which are near to the more rigid structures, [illegible] likely to be detached by coughing [illegible] he lung. Thus it is that the early dust deposits are mostly found near to blood vessels These deposits appear to be in the interstitial tissue and Hulse believes this to be the main mechanism by which deposits are formed, being more important than the deposition of phagocytes in the lymphatic system.

[illegible] move slowly. Powdered carmine administered by [illegible]

hour later found practically all the [illegible] attached to the alveolar walls A week later, 65 per cent of the dust-laden cells were detached from the alveolar wall. Mavrogordato[291] found that cells carrying carbon are eliminated from the alveoli more easily than those carrying silica but that they move mainly towards the ciliated epithelium of the bronchi. Soot inhaled by rabbits and collected by phagocytes was found only in the alveoli and inter-alveolar spaces even 87 days after its inhalation. These observations support Mottura's picture of alveolar phagocytes moving only towards the bronchi and of the passive penetration of the alveolar wall by extracellular dust particles; penetration of the wall by soft soot particles would then be infrequent.

Studies of phagocytosis in tissue cultures of fowl leucocytes[283] indicate that only monocytes, the largest (15–20 μ diameter) type of white cell which has a granule-free cytoplasm, will ingest silica particles, other leucocytes are indifferent even when in intimate contact with the silica. As the phagocytes age, fat globules normally appear in the cytoplasm and enlarge The fat reduces the motility of the phagocytes and also their ability to ingest silica. In these studies the formation of fat globules was considerably retarded in cells engorged with fine silica particles. These cells remained intact longer than other [illegible] ") and they tended to lose their motilit[illegible] [illegible]udied by others.[303, 304, 305] [illegible] using tissue cultures of spleen from chick embryo, found much fatty degeneration when silica was ingested

CHAPTER 10

SILICOSIS

Silica is encountered in many industries Sand is used, for example, in the moulds for steel casting, calcined flint in the manufacture of white ornamental cements, kieselguhr as a polishing powder and sand and sandstone in the manufacture of heat-resisting bricks (ganister bricks, silica bricks) Sandstone and granite, both of which contain quartz, are quarried as building material Because of its wide distribution in the earth s crust, silica is encountered in most types of mining Gold tin and copper occur in quartz-bearing rock and the strata which flank coal measures often contain free silica Silica is very hard and it shatters into fine dust when siliceous rock is drilled or blasted Fine dust is also produced by the abrasion of silica particles on one another and it may be formed in sand conveyors for example

Silica is very often present in the dust of raw materials from which metals and other materials are extracted and it may there represent a hazard For example, Moller and Gudjonsson,[91] who investigated the industrial diseases resulting from the handling and electrolysis of cryolite (sodium aluminium fluoride), stated ' the conclusion is unavoidable that the disease of the lungs was due to the quartz-laden dust in the factories '

The Silicotic Human Lung

Many detailed descriptions of the silicotic human lung have been published (see, e g Middleton,[873] Gardner[308]) Silica is carried by the cells towards the lymphoid tissue within the lung and the tracheobronchial lymph nodes The concentration of the particles results in the proliferation of the connective tissue cells and this narrows the lymphatic channels so that the elimination of particles is hampered Silica inhaled subsequently is thus removed less readily so that the mobile phagocytes now accumulate along the lymphatic trunks Here proliferative changes are initiated and more nodules are formed The first lesions are thus found mainly in the lymphoid tissues

When the disease is not complicated by tuberculosis the lung retains its normal shape and size but its weight is considerably

increased, it may be twice that of a normal lung Tuberculosis results in a contraction of the tissue with loss of bulk.

The condition of the lungs in simple silicosis, as revealed by X-rays, is one of simple nodulation According to Gardner,[309] the *nodulation is evenly distributed throughout the lungs* This condition does not incapacitate the worker. There may be massive areas of conglomerate fibrosis superimposed on this uniform nodulation *in which case the worker suffers from dyspnoea and is unable to* do heavy work. A dangerous condition ensues if tuberculosis intervenes. X-ray photographs may reveal discrete nodulation years after a miner has left his *occupation with a normal X-ray* picture, even in the absence of further exposure to dust or infection.[310]

Silicosis alters the consistency of the lung and the tissue offers increased resistance to sectioning. The cut surface shows scattered, roundish, greyish-black nodules which vary in density but are mostly about 2–5 mm in diameter Occasionally the nodules show a central bronchiole or blood vessel Varying degrees of emphysema are seen in the intervening tissue Cavities, resembling tuberculous cavities, may be present.

Pleural adhesions are common in the silicotic lung. They may be massive and associated with a greatly thickened pleura, or less dense, when the lung surface presents a finely nodular appearance. Over most of the subpleural nodules there is a central, whitish zone of thickened pleura and an outer, greyish-black zone.

Silica content of the silicotic lung

There often appears to be little correlation between the extent of damage in the silicotic lung and the amount of silica the lung contains.[311] Quartz may be present in lungs which are not silicotic.[312] One observer found that the average value for the silica content of the lungs from 7 sandblasters was 1·8 per cent of the dry weight; the lungs from 14 haematite miners without silicosis contained 1·7 per cent silica, and the lungs from 8 other cases of silicosis 1·7 per cent silica.[313] Fowweather[314] found 6·3 per cent silica in the lungs of an ex-coalminer without gross silicosis and 2 per cent silica in lungs which showed no fibrosis whatever, but 5 silicotic lungs gave figures below 1 per cent In another group of lungs from coal miners the degree of fibrosis was correlated to the number of quartz particles in histological sections and the silica content obtained by chemical analysis.[317]

Andrewes[315] analysed a silicotic lung in portions *The dried lung* had an overall ash value of 3 per cent In the most affected part of *the lung the ash contained only* 24 per cent total silica as compared with 36 per cent for the ash of the remaining tissue But analyses

of the lungs of Rand gold miners[316] show that, whereas the lung of an individual not unduly exposed to siliceous dust may contain up to 0 25 g of dust, that of a miner who has rapidly-developed silicosis may contain 15 to 20 g When the lungs collect a heavy load of silica, the lymphatics are affected to such an extent that the strain put on the heart results in rapidly-developing heart failure

Th ... specific lesion ... characteristic whorled nodules ... quarry work best seen in the lungs of stonemasons and quarry ... inhale silica dust inhaled sandstone dust[318] These workers usually inhale silica dust which is only slightly contaminated by other dusts A very chronic lesion is composed of inert, hyalinized, fibrous material There is no evidence of cellular activity except, perhaps, at the surface The fibres tend to be concentrically arranged and the outer fibres are woven into a heavy collagenous capsule Single nodules are less common than conglomerate lesions

Analyses of the protein of the hyaline substance of silicotic nodules (human and rat) show that the different amino acids are not present in the same proportions as in collagen[319] The analyses would correspond to that of a mixture of collagen, α-globulin and β-globulin in the ratio 4 3 3

The densest fibrous tissue in a nodule surrounds the centre and around it is a region of younger fibrous tissue[273] The centre of the nodule is looser in texture and is less definite in structure; it may be necrotic or even calcified[308] According to Policard,[320] tissue which becomes fibrosed by the action of dust becomes impregnated with calcium which is probably combined with protein It is the calcium complexes which are radio-opaque and cause the X-ray shadows

The manner in which the silica particles collect apparently from a wide area of lung tissue into one region is remarkable A silica brick maker worked for 15 years before he died of pulmonary tuberculosis *In sections of the lungs only one silicotic nodule was found and only around this nodule were there any silica particles*[260] The total amount of silica in the lung was so small as to be indetectable by chemical analysis

An ashed histological section of a nodule (*Fig* 10 1 B) reveals an outer halo of dust surrounding a clear zone which contains little or ... [313, 315] The capsule of fibrous tissue in the human lesion is, ... this is in remarkable contrast to ...

(A)

(B)



Fig 10 1 Silicotic nodule in lung of a metal grinder showing characteristic silica pattern with outer halo and clear zone representing capsule. ×60

(A) Haematoxylin and eosin (B) HCl-insoluble ash (dark field)
(Belt & King, *J Path and Bact*, 51, 263, 1940)

The reaction to silica in a nodule is progressive[308] After the nodule is formed, the silica is encapsulated and there is further development of the lesion New nodules are not formed, however, if [illegible]

in some areas but not in others In sections, the nodules do not appear to be "crowded together and touching one another, instead they are embedded in a matrix of diffuse obliterating fibrosis"

The primary cause of the whorled form of the silicotic nodule is the agglomeration of silica-laden phagocytes The remarkable property of the silica particles which causes the phagocytes to congregate does not appear to be shown by other materials to nearly the same extent One description of their formation[308] states "The apparent cause of the nodular form of the silicotic lesion is the localization of the irritant Under polarized light masses of silica particles are visible in the centres of mature fibrous nodules In following the evolution of these lesions it has been observed that phagocytes containing fragments of silica tend to collect in focal areas and that proliferation begins when the local concentration of the irritant becomes sufficiently intense The effect of silica upon the [illegible]

manner or move very slowly into the lymphatic system There is no tendency to concentrate non siliceous particles Proliferation is limited to the number of cells necessary to ingest the foreign bodies"

Grading of silicosis

In the United States silicosis is considered to develop in the three following stages[274]

Stage 1 Few and indefinite symptoms Working capacity unimpaired

Stage 2 Shortness of breath on exertion working capacity diminished, chest expansion decreased

Stage 3 Slight exertion causes distressing shortness of breath Cough is frequent Working capacity is seriously and permanently diminished Chest expansion is greatly decreased There is usually a loss of body weight increased pulse rate, dilated heart and tuberculosis

The X-radiographs show changes which correspond to these stages

Stage 1 Small discrete mottling due to the shadows of the individual nodules.

Stage 2. Generalized mottling with occasional larger but limited opacities due to irregular pleural thickening or to localized aggregates of nodules.

Stage 3 More intense mottling with large, dense shadows due to areas of fibrosis and conglomerations of nodules.

Belt and King[321] graded silicotic lesions in animals and in man according to the following scheme:

Grade of fibrosis	Description of lesion
1	Cellular, loose reticulin network, no collagen
2	Cellular, compact reticulin with or without a little collagen
3	Slightly cellular, fibrosis predominantly collagenous
4	Acellular and wholly collagenous
5	Acellular, collagenous and confluent

Whole lung sections

Gough[322] has perfected a method for preserving and mounting sections of a complete lung which is ideally suited to the study of silicotic lungs The sections are thin enough to be examined microscopically but are also useful for inspection with the unaided eye They are usually preserved in their natural colour by using glycol derivatives although certain staining techniques can be applied when necessary The sections are mounted on paper and can be stored in book form Together with radiographs taken during life, they represent a valuable record of the progress of the disease.

SILICOSIS IN ANIMALS

Laboratory methods

Dust is introduced into the lungs experimentally in two ways Small animals (rats, mice, guinea-pigs and rabbits) may be placed in dust clouds, or the dust may be injected into the trachea

The several types of apparatus which have been devised for inhalation experiments have been reviewed by Wright.[323] The most successful are the tumbling box and Wright's dust-feed mechanism The *tumbling box* is a rectangular, rubber-lined box through which air can be drawn (Fig. 10 2) Lumps of the material from which dust is to be made are placed inside and the box is slowly revolved.

This apparatus is particularly successful with hard materials such as massive quartz and carborundum and since nothing but the material is put into the box dust is formed with minimum contamination *Wright s mechanism* is a device for re suspending preformed dust

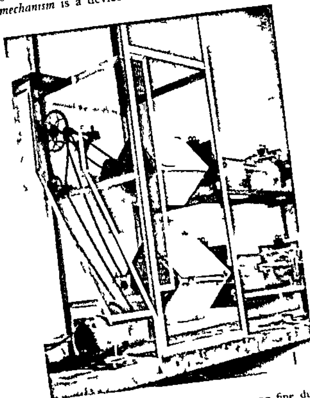


Fig 10 ? Tumbl ng boxes f r preparing fine dust from lump material

The boxe wh h a e l ned w h s ft rubber are rotated l owl The lumps f n a er al at rade ne en he produ ng a fine dust wh h d awn fr m the boxes by a urrent of a r and taken through unnel n a n ng exper men al an n als

The dust is packed hard into a hollow cylinder and its surface is continually scraped by an electrically driven knife edge An air jet disperses the dust as it falls

In the inhalation experiments the dust is administered in a manner resembl ng as nearly as possible that in which it is received by the

industrial worker The atmospheric concentration is necessarily higher, however, because the duration of the experiment is limited by the short life-span of the animal. The method suffers from the disadvantage that quantitative experiments are difficult to devise, since not only is it impossible to maintain a dust cloud of constant characteristics (particle size range and concentration) but variations between the animals mean that the volumes of air, and consequently the amounts of dust, inhaled must vary.

Intratracheal injections[23] are made by exposing the trachea of an anaesthetized rat and injecting into the trachea a suspension of the dust in saline The incision is then closed by a suture. Up to 200 mg of the dust in 1 ml of fluid can be injected, but the maximum amount depends on the type of dust The dust is forced into the alveoli in much larger quantities than can happen naturally and the lymphatic drainage is quite unequal to the task of emptying the air-sacs, the degree of retention is therefore high and the method can be made reasonably quantitative Many more animals can be dealt with by intratracheal injection than by the inhalation technique but the percentage of animals which survive is smaller.

Belt and King described the reaction immediately after the administration of dust by intratracheal injection. The bronchi and bronchioles are more or less flooded with dust and breathing is suspended for 20–40 seconds Afterwards, gasping breathing results in the introduction of innoculum into each lobule of the lung in a quantity which corresponds to the volume of its tidal air. Perhaps a quarter of the air sacs are filled with dust. Later the distribution alters and small dust nodules are formed. Eventually the dust deposits thin out and break up into smaller aggregations stretched along the alveolar septa Only a small part of the total dust reaches the lymph glands The maximum deposit in the glands is found quite early, perhaps in the third week, and lesions may appear in the glands well in advance of those in the lung

The effects of a number of siliceous dusts on lung tissue have been studied by both the injection and the inhalation methods The overall picture is the same whichever technique is used but differences of detail have been noticed [324]

The reaction of the lungs to quartz

The effect of inhaled quartz on the lungs of rats has been described by a number of observers Parts of a section of the lung of a rat which had inhaled silica dust are shown in Fig 10 3. The following is a summary of the findings of King, Wright, Ray and Harrison [324] After 180 days, histological sections of the lungs showed slight thickening of an occasional alveolar wall and mild reticulinosis of the

hilar glands but there was no focal reticulinosis of the lung itself which could be regarded as a nodule A few focal collections of dust laden phagocytes were traversed by a network of fine reticulin fibrils after 220 days These early nodules were rounded, never larger than 345 μ and usually were associated with small blood vessels



Fig 10 3 Photomicrographs showing silicotic nodules in a section of the lung of a rat which had inhaled quartz dust (Reticulin stain A × 90 B × 200)

After 300 days the picture was one of typical nodular silicosis The dense rounded nodules consisted now of collagen with a few fibroblast nuclei but no phagocytes Both the number and the size of the nodules increased during the next 100 days Rats which were still

receiving dust up to the time of death had both early and advanced nodules. There was no evidence of abnormal inflation (emphysema) of the air spaces where respiratory exchange occurs.

Administered by intratracheal injection, quartz produces small, rounded collections of dust cells within a loose network of tangled reticulin fibres in 30 days.[325] These nodules lie mainly near the smaller vessels and the bronchioles; some are intra-alveolar. By the

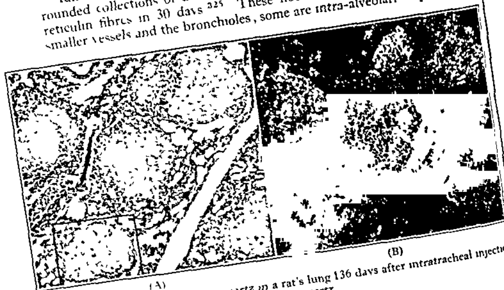


Fig. 10.4. Nodules produced by quartz in a rat's lung 136 days after intratracheal injection of 50 mg. of quartz.

(A) Stained haematoxylin and eosin. ×22
(B) Ashed section washed with HCl (dark field)
(C) Marked area of A stained for reticulin. ×100
(D) Ashed section washed with HCl. ×100
(Belt and King, *J. Path. and Bact.*, **51**, 263, 1940.)

60th day fibroblastic nodules containing coarser and denser reticulin fibres and a few collagen fibres make their appearance. The lesions contain but few cells by the 120th day and are completely acellular and fully collagenous by the 240th day. Thereafter there is a tendency for the nodules to conglomerate.

Electron microscopic studies[650] show that silica causes the cells of the alveoli to multiply and to form a continuous alveolar covering. The cells become modified; the mitochondria, after a short phase of hypertrophy, become thinner and less common. The vacuoles, fairly large in normal cells, become smaller, flatter and more numerous. The cells eventually become more like fibroblasts.

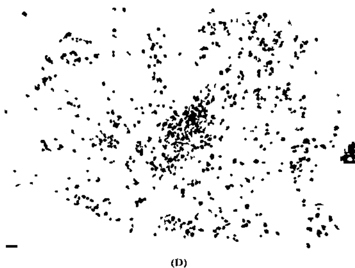
While the silicotic nodules produced in animals by the intratracheal injection of quartz resemble the human lesions in general

(C)



(D)

(C)



(D)

morphology and in distribution, they are smaller, perhaps because the large amounts of dust injected result in less chronic lesions; they are less hyalinized and less contracted.[423] The fibres, which form a network rather than a concentric pattern, are finer. The lesions begin as a cluster of silica-laden phagocytes. Sections which have been micro-incinerated, then treated with hydrochloric acid to remove substances other than silica, reveal the silica particles scattered fairly evenly throughout the nodule (Fig. 10.4) and show no evidence of the encapsulation which is found in the human nodule (Fig. 10.1). In experimental animals the size of a nodule is roughly proportional to the amount of silica it contains.

FACTORS WHICH AFFECT THE FIBROGENIC ACTIVITY OF SILICA

Infection

The importance of infection in the rapid development of silicosis has been repeatedly emphasized. Strachan's description[316] of silicosis as it is seen in the Rand illustrates this. The composition of the dust which is inhaled by miners in the Rand gold mines is comparatively simple and the dust contains a high proportion of quartz. In recent years stringent precautions have been taken against dust and the amount inhaled is small. Simple silicosis takes 5–8 years to show its first manifestations, the lungs usually showing chronic bronchitis with a moderate degree of emphysema, possibly discrete silicotic islets and enlargement and fibrosis of the root lymph glands. With continued exposure to dust, the number of islets increases and the dust-laden phagocytes continuously accumulate around and enlarge the lesions.

If there is no further exposure to the dusty atmosphere, the disease is self-arresting; after a few years the accumulations of phagocytes disappear and the lesions do not increase in size or number. This is the picture of a relatively non-infective process. If infection—pneumonia or tuberculosis—intervenes, then extensive fibrosis rapidly follows. In the Rand, when radiographs of a lung indicate a rapidly-developing silicosis, it invariably means that tuberculosis is superimposed. Sweeny, Porsche and Douglass[311] found tuberculosis in nearly all silicotics and suggested that it changed the disease from a benign to a progressive form. Capelle[326] emphasized the unfavourable prognosis when silicosis is superimposed on tuberculosis. Kettle[327] stated that dusts which produce silicosis produce a medium in which tubercle bacilli flourish and subsequent work seems to have confirmed this. He, and also Cummins[328] carried out experiments *in vitro* which appear to support this view. Mice

show little susceptibility to tuberculosis. Gye and Kettle[244] inoculated mice with tubercle bacilli and silica and found "an enormously greater proliferation of bacilli" in these animals than in controls which received only bacilli. "The silicotic lung", Kettle[329] stated, "appears to be a more favourable medium for the growth of the tubercle bacillus than the normal lung, not because it is fibrotic, nor because its lymph drainage is interfered with, but because it contains silica." In many cases, Kettle[330] claimed, "apparently pneumoconiotic lesions were really infective from the beginning". He also believed that silicotics are predisposed to pulmonary tuberculosis. Others[618 619 620] have shown experimentally that dead or attenuated tubercle bacilli in the presence of silica will produce proliferating lesions and[618 621 622 633] that latent tuberculous infection may be reactivated by silica to progressive tuberculosis.

Cooke[331] stated that 75 per cent of silicotic patients also had tuberculosis but that it was often difficult to find tubercle bacilli in the sputum and the inoculation of guinea-pigs was necessary to detect the disease. Gardner[308] has emphasized that tuberculosis in silicotic persons is a modified disease. The usual symptoms of intoxication are not observed and tubercle bacilli may be absent from the sputum. It is a chronic disease and does not seem to be transferred to contacts. Tubercle bacilli are only abundant in fresh lesions; they are difficult to demonstrate in mature lesions. Among sandblasters, Bergerhoff[264] found more tuberculosis in workers with advanced silicosis than in those with early or slight silicosis. Gardner[308] believed that infection, particularly pneumonia, caused lesions to coalesce.

Sundius, Bygden and Bruce[332] considered that silicosis was not generally associated with tuberculosis in Sweden. Examining sections of silicotic human spleen, Belt[235] could find no evidence that they represented the combined effect of silica and tuberculous infection (but see also King and Belt[333]). Orenstein[334] did not believe that there was an increased incidence of tuberculosis in silicotics and criticized the evidence of some others as being due to erroneous diagnosis. Pope[335] replied to Orenstein, however, quoting the tuberculosis death rate among stonecutters (U.S.A.) as 1,152 per 100,000, ten times that of similar groups in the same community, and Gardner[308] fully described evidence which appears convincing.

When the sericite theory was under discussion, it was reported[336] that the inhalation of sericite dust aggravated tuberculosis. Even immunized animals became infected after inhaling the dust. Quartz dust was said to have no effect. It has been suggested[607] that

dust, not specifically silica dust, may affect the ability of macrophages to destroy bacilli or inhibit their growth. The relation of coal mine dust to tuberculosis is discussed in Chapter 13.

Tests with isonicotinic hydrazide (Isoniazid), which is known to be chemotherapeutically effective in the treatment of tuberculosis, carried out on a selected group of miners with pneumoconiosis, [illegible]

[illegible] when they are infected, the disease runs a normal course[338] The silicotic nodules are very resistant to the infection *In vitro* experiments indicate that neither particulate nor colloidal silica influences the growth or morphology of Type III pneumococci.

The relative fibrogenic activity of different varieties of silica

It has been stated[339, 340, 341, 342, 343] that severe silicotic lesions are not produced by amorphous forms of silica However, Gardner[228] found amorphous silica active and Carleton[275] found it more active than crystalline forms Silicosis is sometimes contracted by ganister (98 per cent SiO_2) workers and silica brick makers who only handle fused products Flint is an amorphous form of silica but there is no doubt that it can produce severe fibrosis.

When quartz, cristobalite, tridymite and fused silica were administered intratracheally to rats in samples containing comparable size ranges, tridymite produced a much more advanced and fused silica a much less advanced fibrosis than either quartz or cristobalite[325]. Completely acellular, fully collagenous fibrosis developed within 60 days of the administration of tridymite, after 12 months very little normal lung tissue was left This fact is inexplicable, particularly as solubility determinations failed to show any marked difference between the four types of silica

The relation between the particle size and the fibrogenic properties of silica dust

Flint dust in samples containing different size ranges between 0 5–8 μ was administered intratracheally to rats to determine the importance of particle size[344] With a dose of 50 mg. for each rat, the severity of the resulting fibrosis was found to increase as the particle size decreased When a dose of dust having a surface area of 700 cm ^{2} was administered in each size range, the maximum damage was produced by particles of 1–2 μ Smaller or larger particles produced less fibrosis Flint in the size range 4–8 μ produced only mild fibrosis even after a year, but particles in the size range 1–2 μ produced almost completely collagenous nodules in 30 days, and maximum fibrosis in 180 days

The lymph glands of these animals were also examined[285]. Those of the animals which received dust 1–2 μ in diameter were more highly fibrosed than the others. The results show that there is a rapid increase in the size of the lymph glands after the dust is given but no further increase after about 6 months. The initial increase is probably due to reactive or inflammatory overgrowth which is later replaced by fibrous tissue of similar bulk.

Amorphous silica of very small particle size (0.01–0.05 μ) produces in rabbits mainly a desquamative catarrh[250] which predisposes the animals to secondary infections and causes a high death-rate. Silicotic nodules are not formed. Very small nodules have been produced in the lungs of rats 243 days after 10 mg. of 20-ångstrom silica had been injected into the trachea.[345]

The effect of cortisone on the action of quartz

The fibrogenesis which is normally induced when quartz powder is injected into the peritoneal cavity of a mouse is suppressed by large doses of cortisone. These effects are not observed in guinea-pigs and the retardation of fibrogenesis is less in the rat and rabbit[282]. Cortisone-injected rats exposed to a quartz-laden atmosphere showed little difference from controls in their initial cellular response to the dust in the lungs[346, 300] but the cortisone prevented or delayed the transformation of reticulin into collagen fibres and slowed the formation and confluence of nodules.

Stacy and King[151] analysed the lungs and lymph glands of rats which had inhaled quartz dust. One group of rats received cortisone also another group did not. The silica content of the lymph glands of the latter group increased markedly with time after silica exposure but that of the former group increased very slightly (Fig. 10.5). The amount of silica in the lungs of the cortisone-treated quartz-dusted rats was slightly greater than that in the control group (Fig. 10.6) but the amount of collagen in the lungs of the latter group was considerably greater than in the lungs of the former (Fig. 10.7).

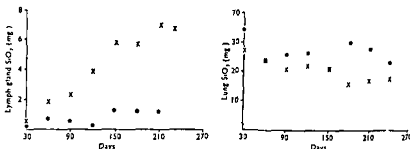
No objective improvement was observed when 8 patients with silicosis were treated with cortisone (100 mg. per day) for 2 weeks.[347]

Influence of other dusts on the fibrogenic properties of silica

For more than twenty-five years investigators have been reporting that other dusts can influence the silicosis-producing properties of silica. Some dusts have been said to retard and some to accelerate the action of silica. Gardner[348] said "The evidence now available makes it seem improbable that a silica hazard is defined solely by the number and size of the silica particles in an industrial atmosphere. The other components of a dust modify its action."

It is possible that the inhalation of alkali, such as sodium carbonate

together with quartz dust renders the quartz much more dangerous. Few animal experiments have been carried out to establish this point and the evidence is derived mainly from industrial experience rather than from experimental tests with animals. Indeed Naesland[343] showed that the alkaline dusts sodium carbonate and calcium



Figs 10.5 and 10.6 Cortisone and developing silicosis
Fig 10.5, average SiO_2 in lymph glands, Fig 10.6, average SiO_2 in lungs
× Control quartz rats, ● Cortisone-treated quartz rats
(Figs 10.5, 10.6, 10.7 are from *Brit J industr. Med*, **11**, 192, 1954)

hydroxide when inhaled by animals produce irritation and necrosis but only slight fibrotic response. When they were mixed with silica no increase in the toxicity of the silica was observed although the animals appeared more susceptible to pulmonary infection.

A particularly severe outbreak of silicosis occurred among workers in an abrasive soap factory. The abrasive soap was manufactured by mixing finely powdered quartzite and anhydrous sodium carbonate. Of 59 persons employed for more than a month in this factory, 13 were known to have died from silicosis or tuberculosis. In some cases death occurred only two or three years after commencement of employment.[157] A characteristic of all these cases was the rapidity with which the disease developed even after only a brief exposure to the dust. Records of these cases are shown in the chart (Fig 10.8).

The effects of an alkaline scouring powder (80 per cent silica, 15 per cent sodium carbonate and 5 per cent moistener, particle size 80 per cent <1 μ) on the lungs of 8 workers in another factory have been described.[349] The sclerosis produced was diffuse rather than nodular. The silicosis was distributed evenly over the lungs and progressed very rapidly. Other records of acute silicosis caused by the inhalation of silica and alkali have been given.[350, 352, 353, 354]

Examples of the protective action of various dusts against the action of silica have been described over many years. Haldane[355] considered that coal dust inhibited the fibrogenic action of silica and he also advocated the use of powdered shale as a protection against the action of silica. The inhibitory action of shale has also been reported

by others [321] Briscoe and others[38] suggested that "a dust such as that of fresh cement might well serve to mitigate the effects of dangerous dusts" Animal experiments conducted by Naesland[343] showed that cement may have an inhibitory effect Other dusts which have been stated to retard the action of silica are coal,[350 356, 357, 358 311 359] aluminium, aluminium hydroxide and, less effective, iron and magnesium [343] The inhalation of calcium sulphate and calcium carbonate dusts as a protection against silicosis has been tried in the Ruhr mines, with disappointing results [360] Sprays of solutions of calcium salts have also been used as antidotes [361]

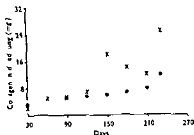


Fig 10 7 Cortisone and developing silicosis graph showing percentage collagen in lungs

In some cases the inert dust has been said to act by stimulating the phagocytosis of the quartz particles Experiments on the effects of coal dust on the

that the rates of phagocytosis of the two dusts are similar to one another [363 364]

Jotten and van Marwyck, using phase contrast microscopy, observed tissue cultures of chick embryo and, estimating the number of dust particles taken up by 100 phagocytes in each experiment, found considerable differences in the rates of phagocytosis They gave the following comparative values for the effectiveness of "protective" dusts in increasing the phagocytosis of quartz particles bolus alba, 18 per cent, gypsum 38 per cent, black metallic aluminium, 58 per cent, limestone and metallic aluminium, no effect They concluded that some dusts can reduce the action of quartz by promoting its phagocytosis

In other cases the action of the protective dusts is thought to be chemical Thus Naesland,[343] using animals, found that the inhalation of cement dust with quartz produced a pronounced delay in the quartz effect He suggested that a basic constituent of the cement, probably calcium or aluminium, reduced the activity of the quartz

indifferent dusts" (coal and glass) had no effect on the action of quartz

The results of animal experiments performed by Ray, King and

FIG 10 8

Duration of employment of persons employed at one factory in manufacturing Abrasive Soap Powder, and the incidence of fatal respiratory disease (Middleton, *Lancet*, 1936, 56) The horizontal lines show the duration of employment and the black rectangles the time of death in the fatal cases that are known

Harrison[365] seem to indicate that pure graphite and clean coal accentuate rather than reduce the pathogenicity of silica. Both dusts are largely eliminated from the lungs and cause only slight reticulinosis but they increase the action of silica which is adminis-

tered simultaneously Small doses of quartz which were insufficient to produce lesions when given alone, produced nodular foci of reticulinosis when administered with large amounts of coal or graphite

Differences in the incidence of silicosis in related industries have often been explained as due to the effects of other dusts Thus Gossner[366] stated that silicosis is widespread in sandstone quarries in France and the Palatinate where quartz and kaolin are abundant but there is no silicosis in certain coal mines where dust originates from calcareous sandstone He suggested that the difference is due to the lime content, lime preventing the combination of silica with the tissues Kettle[367] stated that some shales which were used in rock dusting and which were believed to be harmless contained 30 per cent free silica He used this example to support his claim that shale has a protective action Again Heffernan[8] stated that ganister brick makers in Derbyshire do not get silicosis although they inhale dust which contains 84 per cent of free silica, the rest being clay He suggested that the clay behaves as a protective dust

Aluminium therapy

Assuming that silicotic lesions are produced by dissolved silica, Denny Robson and Irwin[368, 369] studied the effects of finely divided metallic aluminium on the solubility of silica, *in vitro* The aluminium reduces the solubility of quartz practically to zero A group of rabbits were caused to inhale quartz dust and massive fibrosis was produced in their lungs but another group given quartz dust mixed with 1% of aluminium powder showed only slight fibrosis

Some investigators[370] found aluminium ineffective in animals King and others[340, 331] did not find the same inhibition when they administered the mixed dusts by intratracheal injection but later,[324] using the inhalation technique, they compared the lesions in the lungs of animals which had inhaled air containing 30,000 quartz particles per c c with lesions in the lungs of animals which had inhaled a similar atmosphere with the addition of 2 per cent of aluminium Quartz alone produced nodular reticulinosis in 200 days but none if aluminium was added After 400 days the reticulin nodules in the lungs of the animals which had received aluminium were but slightly more advanced than those in the quartz group which were examined after 200 days Chemical analyses showed that the lungs of both groups contained almost identical quantities of quartz Other tests[371], carried out by intravenous injection into rabbits of quartz and quartz plus aluminium or aluminium hydroxide, were also interpreted as proving that both aluminium and aluminium hydroxide are inhibitory

The action of the aluminium is presumably due to its forming a

coating of alumina on the silica[324] since aluminium-treated quartz will adsorb aurine from solution whilst untreated quartz is unaffected Heppleston[372] thought the aluminium relieved bronchial spasm.

The application of aluminium therapy to the prevention and relief of silicosis in man is discussed in Chapter 16.

Blood picture in silicosis

The blood picture in silicosis is stated to be fundamentally normal, but statistically significant increases in eosinophil and monocyte *counts have been found*[373] *and a mild relative lymphocytosis, the* result of a leucopenia, has been correlated with the stage of development of the disease[374] The erythrocyte count is unchanged.[374]

In Rhodesia, the erythrocyte sedimentation rate among the normal population was found to be 11·4 mm, for African copper miners with simple silicosis 19·1 mm, and for those with massive fibrosis 53·1 mm[310] The sedimentation rate was considered to give good evidence of the activity of the lesions

Changes in the blood proteins have been recorded.[375] Vigliani, Boselli and Pecchiai[376] described increases in serum globulins, [illegible] but only [illegible] increase [illegible] fibrosis. [illegible] hrombin activity and alterations in the plasma proteins have been reported in cases of silicosis[377] The composition of the serum proteins in *silicosis has been studied by electrophoresis.*[633] Changes in the lipids of the blood in silicosis have been investigated.[632, 634]

CHAPTER II

THE SOLUBILITY THEORY OF SILICOSIS

The theory of mechanical trauma

It was believed until recently that dust particles damage the lung because they pierce and abrade the tissues "The more jagged and angular the particles, the greater is their power of mischief" "It seems reasonably certain that hard, gritty dusts composed of sharp and jagged particles are the ones especially to be feared"—Landis[4]

From time to time other theories were introduced to explain the pathogenic effects of silica Aldridge[3] in 1892 wrote "it is not to be lost sight of that other qualities of dust, besides their shape, play a considerable share in their morbid effects upon the tissue For instance, density is of great importance, and so is the degree of their divergence as regards organization and chemical constitution from those of the tissues penetrated Thus, it is seen in the case of lime

The sericite theory

Undoubtedly the most startling development in the mechanical theory of silicosis was introduced by W R Jones[379, 380] in 1933 He made petrological examinations of sections of quartz-containing rock from the Rand mines and revealed that the quartz crystals were

Australia, where there is a high incidence of silicosis although the quartz content of the rock is not unduly high, sericite and another fibrous mineral sillimanite were abundant. Sericite was found

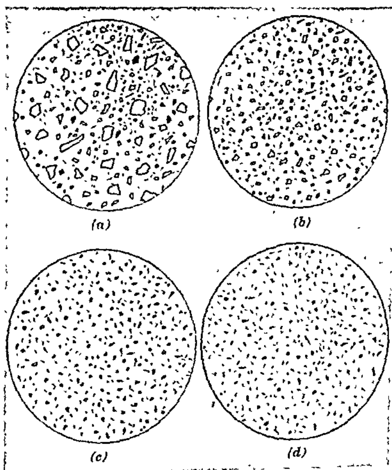


Fig 11 1 Sketches to illustrate the increase in the ratio of fibres of sericite to quartz particles at different periods after blasting

more slowly than the quartz particles (Fig 11 1) and he regarded

cutaneous injection of sericite although quartz gave considerable fibrosis when injected Similar negative results were reported by others,[383,384] and analyses of certain rocks[385,386,387] which produced dust known to cause silicosis showed that sericite was absent, or

The piezo-electric theory

One theory[388,389,390] which attracted considerable attention for a short time ascribed the pathogenicity of quartz to its piezo electric properties The crystalline particles in the lung being subjected to pressure changes during respiration were sources of electric currents which, it was thought would damage the cells This theory was advanced in spite of the fact that fused quartz was known to be fibrogenic It was later shown[391] that tourmaline, which gives a piezo electric response as great as that of quartz and barium titanate and aluminium orthophosphate which also have piezo electric properties, would not produce fibrosis in two years when injected intravenously into rabbits Tridymite, which has no piezo-electric properties will produce fibrosis

The protein coagulation theory

Hounam[392,393] sought to relate the fibrogenic properties of dusts to the charge which they carry He estimated the negative charge on dust particles by adding methylene blue which carries a positive charge, until the dye was no longer adsorbed Positively charged dusts were treated with Biebrich scarlet He concluded that

charged dusts
eoli but that
only after they

had been transported in the lymph

The alkali theory

At one time Briscoe and co-workers attached importance to the alkali which is formed by the hydrolysis of mineral silicates, particularly at freshly-fractured surfaces. It was shown that dust derived from granite, for example, released potassium hydroxide when placed in water. This alkali, it was thought, might be capable of

it nearly

irrelated

, cannot

account for the fibrosis which is produced in animals by pure quartz

The carbon dioxide theory

A theory advanced by Edge[394] to explain the damage caused by silica drew attent

many specimens c

carbon dioxide.

31°C, the inclusions would become gaseous at body temperature and Edge estimated that the pressure would be half a ton to the square inch He visualized tissue damage produced when this pressure was released by the dissolution of the particles in the lung.

The theory of damage by freshly-fractured surfaces

hemical reactivity of

that air-borne

before they enter the alveoli [399]

The theory which relates the activity of fresh surfaces to tissue damage has been severely criticized by Wright,[400] who emphasized the difficulties of obtaining experimental evidence to prove or disprove it He believes that this theory, which has had many adherents, is untenable Certainly, fibrosis can be caused by the inhalation of dust which is not freshly prepared; Gardner[401] successfully produced silicotic lesions in animals by *allowing them to inhale* the dust produced by stirring up commercial ground silica, but freshly prepared dust was believed by others[402] to have a higher pathological activity. A decrease has been noted in the solubility of silica dusts after storage [403]

Theory of protein adsorption

One possible mechanism by which silica may interfere with the normal tissue metabolism is by the adsorption and possibly the alteration of some essential component from the cytoplasm of the cells on to the silica surface. When protein is adsorbed from solution on to quartz its structure is changed[402] and it has been suggested, for example, that the toxic action of quartz may be a result of a foreign protein reaction in the tissue. Undoubtedly adsorption could occur. Proteins are certainly adsorbed on to silica surfaces from aqueous solutions and from cerebrospinal fluid, ascitic fluid and serum (Chapter 6).

If the adsorption of protein on to silica surfaces is responsible for the fibrogenesis which occurs in silicosis a difference must be demonstrable between the adsorptive properties of silica and those of non-pathogenic materials. The adsorption process has not been widely studied, but no such difference has yet been found. Indeed the adsorption isotherms drawn from data recorded when proteins are adsorbed on quartz markedly resemble those obtained when proteins are adsorbed on kaolin.[405]

The behaviour of carborundum dust in the body also seems to indicate that this hypothesis is untenable. There is no significant difference between the surface activity of quartz and carborundum. The recent studies on the solubility of carborundum dust have shown that the dust particles are coated with a layer of silica (Chapter 3). The ability of carborundum to adsorb substances from the cytoplasm will resemble that of silica. Since carborundum has not been found to cause gross fibrosis in the lung tissue, it must follow that the pathogenic properties of quartz are not due to the surface activity of the particles.

The Solubility Theory

Shortly before Jones introduced the sericite theory, several research schools in England and America were investigating the effects of silica and other dusts on tissues by using test animals. Their results cast some doubt on the feasibility of the Mechanical Theory. Gardner[406, 407] found practically no change in the lungs of animals which had inhaled carborundum dust for three or four years, although particles of carborundum dust are as hard and as sharp as those of quartz dust. Gye and Purdy produced necrosis of the liver in mice by injecting colloidal silicic acid,[225] a result which suggested that silicic acid could exert a toxic chemical action on the tissues, from which it was reasonable to assume that the action of silica particles was in fact the action of the solute formed when the silica dissolved in the tissue fluid. Kettle[408] embedded a collodion sac containing silica in a rabbit's flank and proved that an inflammatory

condition was induced in the tissue which resembled the early effects of injected quartz. This effect could only have been produced by a solute which had passed through the collodion sac, and this again suggested that the damage to the tissue in silicosis is due to a toxic substance dissolving from the dust; the toxic substance [illegible] to be silicic acid.

[illegible] by Kettle[409] was described by [illegible] soluble [illegible] osis. [illegible] osis [illegible] ated [illegible] Kettle injected crystal [illegible] of this silica [illegible] He then injected a specimen of this silica [illegible] fibrosis. Nearly with ferric oxide and found that it did not produce fibrosis. Nearly half of the second sample was ferric oxide so that neither its shape nor its hardness nor its particle size was likely to be identical with that of the untreated silica, and Kettle designed his experiment not to study the mechanism of fibrosis but to explain the inactivation of the asbestos fibres in asbestosis bodies. However, the influence of this experiment on the acceptance of the Solubility Theory cannot be doubted

The Solubility Theory of silicosis assumed that the damage caused to the tissues of the lungs and the lymph glands by dust was due to the toxic action of the silicic acid which is produced by the dissolution of silica or silicates in the tissue fluids. It should follow that the dusts which produce the most damage to the tissue are those capable of releasing most silicic acid; that is, those which dissolve most rapidly In several laboratories, efforts were made to measure the solubilities of dusts. Some of the early work was carried out before many of the factors which influence the solubility rate had been studied These factors have been discussed in Chapter 5. In many cases the classification of dusts as "highly soluble" or "sparingly soluble" must have been fortuitous but often the correlation between the fibrogenic activity and the measured "solubility" was remarkable. As an example, figures are quoted in Table 11 1 from a paper by Briscoe, Matthews, Holt and Sanderson

Again, King and Belt[78] extracted a fixed weight of siliceous materials with a fixed volume of plasma under stated conditions and compared the amounts of silica in solution after a fixed time interval. Values obtained in this way have been referred to as the "comparative solubility" of the dust His results showed that the amounts of silicic acid which passed into solution from most pathogenic dusts, such as quartz and flint, were greater than that from the least pathogenic dusts such as shale The comparative solubility values obtained under the conditions King used were about 10 mg. SiO_2 in 100 ml. of solution for quartz and 1–2 mg. SiO_2 in 100 ml. of

TABLE 11 1

Comparative Solubilities of Certain Mineral Dusts and Powders

Mineral	Dissolved silica mg SiO_2 per g of mineral extracted with 100 c c water at 100° for 3 hours
	mg
Asbestos	25 2
Flint (pure)	24 0
Quartz	5 2
Felspar	3 4
Sericite	2 2
Kaolin	0 8
Flint (calcined commercial)	5 7

solution for shale Briscoe and others found values of the same order for dusts, using water as the solvent

Anomalies of the simple Solubility Theory

When the results of recent investigations on the dissolution of silica are considered, it is not surprising that King[411] later found that the comparative solubility values he obtained were no guide to the degree of pathogenicity of some other dusts Gardner also found that the very finely divided silica condensate, 20-ångström silica was harmless to the lungs of animals in spite of its high comparative solubility value, and sandstone is comparable with quartz in its ability to produce fibrosis, although its 'solubility" is much lower than that of a harmless shale In one of his reports Gardner stated "As far as this part of the work has progressed, it has been impossible to establish any correlation between the degree of solubility *in vitro* and the capacity to provoke reaction in the living body "

The later research on the anomalous solubility characteristics of silica indicated that silica normally has a layer of silicic acid adsorbed on its surface, it is this silicic acid which dissolves rapidly when silica is placed in water, and after a period of a few hours, accounts for most of the silicic acid in solution Once this layer is removed, solution is a slow process The "solubility" determinations which were made on dusts and powders measured mainly the extent of this silicic acid layer which is related to the surface area of the dust Plainly the comparative solubility values represent the amount of

silica which dissolves in the first few hours during which the dust is in the lung The values bear no relation to the "solubility" of the dust once the silicic acid layer has been removed Consequently these comparative solubility values give no indication of the amount of silicic acid which would dissolve once the dusts had been ingested by a cell

[illegible]

accumulation of phagocytes . . ."; "rat lesions begin as a cluster of silica-laden alveolar phagocytes" [413] The silicic acid which is formed before the dust particles are absorbed into the cytoplasm of a cell, and possibly that which is formed in the cell before it has migrated to one of the agglomerations of dust-laden phagocytes in the lung or in a gland will not, then, induce fibrogenesis. No comparison has yet been made of the rates of solution of the ingested dusts in the cytoplasmic fluid These considerations mean that no criticism of the Solubility Theory can be based on "solubility" values so far available, any more than the values can be used as evidence in favour of the theory

An extended Solubility Theory

Studies described in Chapter 6 have shown that silicic acid can combine with collagen and that, if the silicic acid polymerizes, it profoundly alters the properties of the protein We will consider the implications of this

In normal tissue, collagen fibres are believed to be formed by the orientation of relatively small, linear, pre-collagen units, this orientation being induced by polysaccharidic sulphates such as chondroitin sulphate (Chapter 7). These mucopolysaccharides are not specific precipitants, fibres have been formed *in vitro* from collagen solutions by the addition of other reagents Even sodium [illegible]

acid is formed by the dissolution of the silica [illegible]
low because the rate of solution of the silica is low and consequently [illegible] $Si(OH)_4$.
[illegible] bodies
[illegible] saccha-
rides being formed In so far as polysaccharidic sulphates are

produced the small collagen units will be orientated by the normal process of fibrogenesis At the same time interaction will occur between the collagen precursors and the silicic acid molecules Once the silicic acid is adsorbed to the protein the local concentration at the protein surface is raised and polymerization can occur The formation and stabilization of the fibres by silicic acid probably requires the two stages of adsorption of small silicic acid molecules on the protein structure of the collagen precursors and their subsequent polymerization

Studies that were made on the adsorption of silicic acid to monolayers of proteins indicated that as the silicic acid is adsorbed and a local high concentration is built up on the protein surface polymerization can occur at these sites even though the concentration of silicic acid is too low in the solution for polymerization to occur there Here then is an explanation of the fact that the small amounts of silicic acid which are formed when the dust particles dissolve in the cells are able to induce fibrogenesis The silicic acid is effective only when it is produced together with the collagen precursors If the silicic acid is formed in the blood or the tissue fluid it is more likely to interact with the proteins of the serum or the lymph or indeed with any of the polar constituents of the tissues Such interaction will represent a mechanism of detoxication

The mechanism of silicic acid induced fibrogenesis which is outlined assumes that the silicic acid is in units which are small enough readily to diffuse away from the cell and that its concentration at the cell surface is so low that no appreciable polymerization occurs Because of the low solubility of silica this will certainly be true The experiments of Cagliotti Liberti and Benedetti (Chap 7) suggest that polymerized silicic acid would inhibit rather than initiate fibre formation The theory assumes also that when the small ortho silicic acid molecules are adsorbed on to the particles of the collagen precursors conditions are favourable for polymerization to take place so that the fibres are stabilized Polymerization is more likely to occur on the collagen structure if the local concentration of silicic acid is high that is much silicic acid is adsorbed if the pH is near to 6 5 and if the hydroxyl groups of the silicic acid which are not linked to the protein are free These three factors may be considered individually

The concentration of silicic acid at the collagen surface is plainly dependent on the rate of solution of the particles in the cell If the particles are of free silica the rate of solution will depend only on their surface area When a large number of small free silica particles is packed into the cytoplasm of the phagocyte the rate of solution will be at a maximum and the concentration of silicic acid will be highest

If the same number of silica particles is distributed between several cells, the concentration of the resulting silicic acid solution will be lower than if the particles are contained in a single cell, and consequently the degree of fibrosis induced is likely to be lower. Here is one possible explanation of the effect of a "protective" dust. If the phagocytes are induced to assimilate a load of mixed dust, the silica particles will be distributed over a greater number of cells so that the local concentration of silicic acid will be lower even if the total dissolved silicic acid is the same. A longer time must then elapse before the concentration at the collagen surface is high enough for polymerization and stabilization to occur.

Silicic acid polymerizes most readily at about pH 6·5. The pH of the tissues generally is 7·4 If there is liberated along with the silicic acid a substance which will tend to increase the pH in the neighbourhood of a cell, polymerization must be retarded, or if an acidic substance is liberated the rate of polymerization will be increased. This may, in part, explain the reported low fibrogenic activity of alkali silicates such as cement and sodium silicate At the same time it must be remembered that most of the simple silicates are fairly soluble in water and in some cases they may dissolve in the tissue fluid before they can be taken up by phagocytes The pH at the surface of quartz particle in water is less than 7.[414]

When quartz dissolves in water only silicic acid is formed The dissolution of a mineral silicate or of cement is likely to produce also one or more polyvalent cations These cations can serve as a link between polysilicic acid molecules or between sites on proteins Either of these reactions would inhibit the combination of silicic acid and collagen precursors because reactive sites would then be filled This again indicates a reason why silicic acid appears to have a lower fibrogenic activity when it is formed in the presence of a polyvalent cation such as calcium, as in cement, or aluminium which has been proved to inhibit fibrogenesis due to quartz, at least in rats Monovalent cations do not act in a similar way. The studies of the characteristics of monolayers of proteins and organic acids have shown that polyvalent ions profoundly affect the properties of the films This again may be part of the reason for the protective action of aluminium and calcium compounds.

If this extended solubility theory is accepted, some of the anomalous experimental results which have been reported can be explained In particular, the very confusing results of experiments designed to demonstrate the effects of other dusts on the fibrogenic activity of silica will be expected because their action is no longer a simple phenomenon it is complex A second dust may act in several ways In the alveoli it may have an irritant effect if it is soluble, increasing

the volume of the extracellular fluid and consequently the probability of other dusts penetrating the alveolar wall In that case it may increase the rate of fibrogenesis merely because it allows more dust to penetrate into the tissues Perhaps this may explain the action of alkali in accelerating the fibrogenesis caused by quartz

Once the dust is taken into the cytoplasm of a phagocyte along with silica particles, it may dissolve to give metal ions which can react with the surface groups on the silica particles forming a protective "insoluble" coating, it will then directly reduce the rate of solution of the silica particles and so inhibit fibrogenesis If the cell takes up particles other than silica, the load of silica in that cell is likely to be less than if there were no other dust, and this too, as we have seen, will help to prevent fibrogenesis

The study of coal miners' pneumoconiosis (Chapter 13), and some other types of mixed dust pneumoconiosis, has suggested that dusts may block the lymphatic drainage system, particularly when some degree of fibrosis has been induced by quartz The effect o to enhance the damage caused by the silica Dusts othe silica may also in themselves induce fibrogenesis Aluminiu particular, has been proved capable of this As the action of an a dust is so complex, the results obtained when mixed dusts are in must depend on many factors such as the relative concentratio the two types of dust and the chemical and physical properties of added dust

The Solubility Theory of silicosis, more than any other, has serv as a guide in the planning of experiments devised to give informatic about the production of silicotic lesions Because of anomalie its usefulness has been questioned and some investigators hav frankly discarded it It seems likely, however, that the theory is fundamentally sound but that it over-simplifies the problem While the extended theory which has been discussed still gives no more than an outline of the process of fibrogenesis, it does suggest that the Solubility Theory, far from being superseded, is still the most satisfactory hypothesis on which to plan experiment

CHAPTER 12

ASBESTOSIS

Asbestos has been used for at least 2,000 years. Pliny[415] A D 23–79 in his *Naturalis historia* described its properties and spoke of the uses of asbestos fabric "A linen has now been invented that is incombustible It is called 'live' linen and I have seen napkins made of it being washed in water The linen is used for making shrouds for royalty which keep the ashes of the corpse separate from the rest of the pyre The plant grows in the deserts and sunscorched regions of India where no rain falls, the haunts of deadly snakes, and it is habituated to living in burning heat." But the material was rare: "When any of it is found it rivals the prices of exceptionally fine pearls The Greek name for it is *asbestinon* . . . this kind of linen holds the highest rank in the whole of the world"

Asbestos is mined by blasting and quarrying. Between 2 and 10 per cent of the mined rock is fibre. The crude asbestos of commerce contains 5–20 per cent of rock, dust and fine fibre which is removed in opening and spinning. The long-fibre yarn (chrysotile fibre-length ¾-inch or more, amosite up to 6 inches) is used for textiles, packing gaskets, felted paper and for goods made from asbestos cement where maximum strength is desirable Asbestos of medium fibre-length goes into paper and board, filter pads, brake blocks, brake linings and asbestos cement The short-fibre (fibre length about ⅛ to ¼ inch) material is useful only for paint, plaster and asbestos cement Asbestos is used extensively as a mineral filler in plastics

The dangerous nature of asbestos dust was recognized only recently In this country the first case of asbestosis to be described was that of a man who died in Charing Cross Hospital in 1900; the second case was reported 25 years later.[416] By 1928 there were still no more than ten cases on record.[417] The recognition that a pneumoconiosis was caused by the inhalation of asbestos dust followed a few years later, after several other cases had been described in England[418] and a heavy incidence had been observed in some German factories [419, 420] About this time Hunter[421] saw 30 cases of asbestosis at the London Hospital in 5 years Wyers[422] has shown

that a sharp decline in the incidence of asbestosis has occurred since the adoption of proper methods of dust control in the factories and the character of the disease has altered it is now manifested in a more chronic form

Composition of asbestos dust

Chrysotile $3MgO\,2SiO_2\,2H_2O$ is the main asbestos of commerce but crocidolite and amosite are also used The native fibrous asbestos is embedded in other non fibrous or micro fibrous minerals such as serpentine and talc Another fibrous mineral the non siliceous

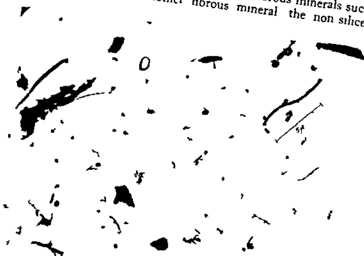


Fig 12 1 Electron micrograph of a dust sample taken by a Thermal Precipitator from the air of an asbestos works
Asbestos fibres are present but there are also many particles of other minerals and amorphous soot particles
Micrograph by Safety in Mines Research Establishment Crown Copyright

brucite $MgO\,H_2O$ sometimes occurs with the asbestos Brucite is of no value as a textile fibre because its fibres are insufficiently flexible

The manufacturing processes entail the breaking up of massive asbestos into fibres In this process the non fibrous material is shattered to give a fine dust having an average particle size much smaller than that of the asbestos fibres The non fibrous dust consequently settles more slowly than the asbestos and the atmosphere of an asbestos mill with modern ventilating equipment contains far

more non-fibrous than fibrous particles. Most samples of air-borne dust collected from industrial atmospheres show few asbestos fibres in the size range which is thought to be of pathological import. In the electron micrograph of a sample taken from the air of an asbestos mill by a thermal precipitator, shown in Fig 12 1, fibrous asbestos particles, non-fibrous mineral particles and the amorphous sooty particles found in the atmosphere of any industrial town can be distinguished

Hurlbut and Williams gave the following analyses for dust collected from the rafters of the different departments of an asbestos textile mill

Dust Produced in the Manufacture of Asbestos Textiles

	Preparation	Carding	Spinning
	Per cent	Per cent	Per cent
Talc	6	9	5
Carbonate	30	27	21
Magnetite	28	21	27
Serpentine	14	29	27
Asbestos	15	8	8
Others	7	6	12

Pathology of asbestosis

Asbestosis is a chronic disease. The lesions take some years to develop. In some circumstances silicosis may develop extremely rapidly and death may occur within two or three years of the first exposure, but such rapid development never occurs with asbestosis

Superficially the lungs of a person who has died from asbestosis resemble the lungs of a victim of silicosis They are hard and incompressible and they adhere to the pleura. X-ray pictures of the chest of an asbestotic patient show the lung fields to be interspersed with very fine, shadowy, round spots. They are mostly undefined but occasionally are sharp and they are denser in the middle and lower regions of the lung. The shadows on the X-ray films correspond to regions in which abnormal connective tissue growth has occurred This growth of diffuse connective tissue is greater in the lower part of the lung.[423]

The fibrosis due to asbestos is much more diffuse than that due to silica [421] Whilst in silicosis there are numerous almost isolated foci, in asbestosis there is a fine network throughout the lungs. Hunter describes the radiographs as having the appearance of ground glass The degree of shadowing present in advanced asbestosis

would have little significance if seen in silicosis [424]. However, Wyers[422] states that the more chronic form of the disease shows up in radiographs as shadows which are coarser and more granular in appearance.

The most obvious symptoms shown by a patient are those of dyspnoea. Tuberculosis may be present but asbestosis is not accompanied by a predisposition to tuberculosis, as is silicosis [425]. Quite often there are no tubercle bacilli in the lungs. Asbestos fibres have occasionally been found in the urine of patients with asbestosis [426]. Half the group of workers with asbestosis which Wyers[422] studied had clubbed fingers.

According to Knox and Beattie[427, 428] who examined lungs from 25 deceased persons who had been exposed to asbestos dust, the severity of asbestotic lesions is related to the time elapsing between the first exposure to the dust and death rather than to the mineral content of the lungs.

A visual examination of a sectioned diseased lung reveals tissue which is interspersed with sharply outlined, air-free, greyish-black areas. When examined microscopically, the lung sections are seen to contain many asbestos fibres which lie in the alveoli and air ducts and in the lymphatics and connective tissue. There are few fibres in the bronchial lymph glands. An asbestos fibre may penetrate the walls of one alveolus into a neighbouring alveolus. The most important position of protective tissue response in the case of asbestos fibres is the terminal portion of the respiratory bronchiole whereas with minute silica particles it is the peribronchial and perivascular lymph nodes [318]. Emphysema is always observed in sections from the lungs of a person who has died with asbestosis.

Strobe[429] found hardly any phagocytes connected to fibres in the alveoli but there was considerable phagocytosis of the disintegration products of the fibres. Gloyne[430], however, frequently observed the ingestion of fibres and bodies by macrophages and regarded this as a normal method for the removal of fibres from the lung. Sundius and Bygden[431] could find only hornblende in the lungs of persons who had died from asbestosis although the persons had handled materials which contained mostly serpentine.

A recent paper on the pathology of asbestosis is that of Lynch [624].

Asbestosis bodies

The characteristic feature of the lung sections from an asbestosis case is the presence of large numbers of peculiarly shaped structures. There may be 8,000 of these asbestosis bodies visible in a section of lung tissue 1 cm ^{2} in area.

Asbestosis bodies form rapidly in the lungs. They have been

found in the lungs of a patient exposed to the dust for only 2 months—and they may appear in the sputum within 5 months of exposure. Asbestosis bodies in the sputum or in the lung do not necessarily indicate a condition of pulmonary asbestosis. Indeed it has been observed[433] that most workers in asbestos factories have asbestosis bodies in the sputum. *Asbestosis bodies were found in the lungs* of one man who had lived near to an asbestos factory for many years but had never been inside it!

[illegible][433] These fo[illegible]ey may be em[illegible] Haddow[433] state that the clumps in the alveoli are almost certainly derived from clumps in the fibrotic areas since the alveoli which contain clumps are always adjacent to areas of advanced fibrosis. Clumps of asbestosis [illegible]ering from [illegible]dicate that [illegible] to a condition of asbestosis.

Originally, there was considerable controversy about the nature of asbestosis bodies. Some investigators believed that they were "essentially derived from, or associated with asbestos and were, in fact, portions of asbestos fibres in the process of alteration and absorption by hydrolysis, either by direct chemical action or by enzymes".[436] Others, such as Cooke,[417] believed that their "results completely negatived the theory that the bodies are asbestos or derivatives of asbestos". Cooke stated that "if organisms—staphylococci, for example—are incubated with a colloidal solution of asbestos they become silicated and resemble asbestosis bodies". He sought to prove that most of the bodies were actually "vegetable" in origin. A report on the discussion which followed a paper describing an early case of asbestosis[437] said: "A second interesting *feature . . . was the presence of a body which some thought was an* aspergillus. The authors of the papers held the view that it was a hyphomycete analogous to that found by Dr. H. H. Scott in batrachians, or that it belonged to the tuberculariaceae, a family of hyphomycetes described by *Ehrenberg in 1818*."

An outstanding investigation of the structure, formation, disinte-[illegible] Beger.[438] A [illegible] Hanover, [illegible] man who had died from asbestosis. Beger had no knowledge of medicine, and stated "I deferred all study of the literature on asbestosis and asbestos bodies, until such time as I should have completed my experimental investigations." In the lung sections which he

[illegible] fibres and [illegible] bodies There [illegible]

Length	(μ)	109	94	87	60	49	46	38	36	35	33	28	25	25
Thickness	(μ)	0 8	0 4	0 3	0 3	0 8	1 0	0 2	0 7	0 3	0 5	0 3	0 3	0 2



[illegible]

There was no relation between the length and the thickness some times long fibres were thin or short fibres thick Very long needles say 120 μ were seldom seen but long needles are easily broken in sectioning By measuring the optical properties of the fibres (refractive indices double diffraction distribution of the optical vectors etc) and by considering other physical and chemical pro perties the fibres were identified as chrysotile

Beger described asbestosis bod es (Fig 12 3) as golden yellow structures sometimes having the shape of a dumb bell but more often in the form of a string of irregularly shaped discs the string of beads form At the ends are club like protuberances An average diameter of the head is given as 7 7 μ and of the shaft 3 5 μ The length is from 10 to 100 times the thickness

Running down the centre of the asbestosis body a fibre or a modified fibre may sometimes be seen Usually the fibre is still

straight but it has reduced rigidity and is less brittle. Occasionally the fibre is curved or even coiled. The coating of the fibre is a gel-like substance.

Electron micrographs[439] of asbestosis bodies collected from the sputum also reveal a central asbestos fibre which is coated with a gel When the gel is removed by micromanipulation, the fibre appears to have transparent edges suggesting that a constituent of the fibre has dissolved. No fibres shorter than 10 μ were found, suggesting that short fibres dissolve completely.

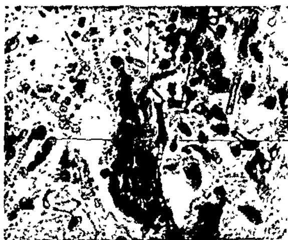


Fig 12 3 Asbestosis bodies (×800)

Chemical composition of asbestosis bodies

Microchemical tests on the bodies show that the gel coating is a protein and that the granules therein are ferric compounds The gel is not removed by hypochlorite and this reagent has been used[440] to separate asbestosis bodies from lung tissue Sundius and Bygden[431] gave the following analysis of an asbestosis body:

Organic matter	31% (S, 0 43%)
Iron oxide	40%
P_2O_5	6 9%
Water	16%
"Asbestos" needle	4 6%

An elementary analysis established that the organic matter was mainly protein. Koppenhoffer,[441] however, thought that the sheath was not composed of protein.

Formation and disintegration of asbestosis bodies

Beger suggests that the bodies are formed by the deposition of

The commencement of the disintegration of the asbestos fibre in the asbestosis body is shown initially by cleavage lines in the cylindrical



Fig 12 4 The first stage in the disintegration of an asbestosis body is shown by cleavage lines in the cylindrical portion of the sheath (× 1,270)

portion of the sheath at right angles to the length of the fibre The heads then show cleavage Finally the asbestosis body disintegrates completely, afterwards nothing remains but a series of granules from which the shape of the original body can be surmised These stages are illustrated in Figs 12 4, 12 5, 12 6

The breakdown of asbestos fibres by the formation and disintegration of asbestosis bodies in the lung is emphasized by differential counts of fibres made on the lungs of 27 deceased persons who had been employed in the asbestos industry [428] The figures shown in



Fig 12 5 The disintegration of an asbestosis body is later shown by cleavage of the "heads" (× 1300)

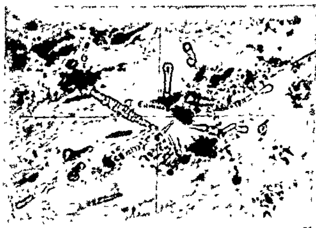


Fig 12 6 An asbestosis body finally disintegrates into a series of granules (× 650)

Table 12 1 indicate that, when the time interval between the last exposure to the dust and death was more than 8 years, there were usually no fibres in the lung longer than 25 μ Fibres in this size range were abundant in the lungs of persons who survived for a

shorter time after the last exposure to the dust Gloyne[440 44] also believed that there were fewer and smaller fibres and asbestosis bodies in the lungs of long standing cases of asbestosis than in the lungs of workers exposed to the dust for a shorter time

TABLE 12 1

Parti le size Distributions Expressed as Percentages of Co nt in the 16–25 μ range

Case No	Sex	Total exposure time Yr	Survival time Yr	Asbestos bodies – +	Mean particle counts					
					Less than 5 μ	5 15 μ	16 25 μ	26 35 μ	36–45 μ	Over 45 μ
3	M	26	0	++	364	193	100	36	21	0
23	M	28	0	+	458	217	100	42	0	0
26	M	20	0	+	510	290	100	51	15	6
9	M	11	0	–	612	389	100	62	18	11
17	M	12	0	+	394	281	100	79	9	2
25	M	8	0	–	627	329	100	38	17	21
12	F	32	1	–	501	257	100	48	0	17
2	M	27	2	+++	689	387	100	33	0	
5	M	28	2	+	433	225	100	50	17	
21	F	33	2	–	573	381	100	14	2	
4	F	14	2	+	627	296	100	62	20	
19	F	8	2	+	522	359	100	41	8	
6	M	22	3	+	421	325	100	51	25	
10	M	9	3	–	510	322	100	50	20	17
14	M	27	4	+	517	281	100	46	18	0
22	M	7	6	–	486	369	100	31	12	2
1	M	23	7	+++	610	487	100	0	0	0
27	M	21	8	+++	786	521	100	22	2	0
20	M	25	8	+++	829	644	100	11	4	0
8	F	27	8	+++	898	591	100	4	1	0
13	M	27	8	+	496	321	100	0	0	1
7	F	6	9	+	611	418	100	0	2	0
28	M	2	11	–	587	292	100	0	0	0
11	M	22	14	+++	720	599	100	0	0	0
24	M	19	14	+++	1 006	707	100	0	0	0
15	M	14	17	–	529	386	100	2	0	0
16	M	10	21	+	647	411	100	9	0	0

(From Knox J F and Beattie J *Arch ndustr Hyg* **10** 30 1954)

The formation of asbestosis bodies has been described as a defence mechanism of the body for the detoxication of asbestos fibres[440 443] The bodies appear to be innocuous Asbestosis bodies were recovered from a human lung then they were injected intratracheally into guinea pigs lungs No fibrosis was produced although the bodies remained in the lungs for a year or more It was possible to produce fibrosis however by injecting asbestos fibres

Experimental asbestosis

Asbestos dust has been administered to animals by inhalation and by intratracheal, intravenous, intraperitoneal and subcutaneous injection. The maintenance of an atmosphere containing a suitable concentration of asbestos dust is not easy. The inhalation chamber used in the Saranac laboratory was a cubical room, length of side 8 ft., in which asbestos dust was thrown into the air by a paddle slowly rotating in a hopper. Since the fibres tend to form balls in the hopper, wire brushes were attached both to the paddle blades and to the floor of the hopper. Animals were kept in this room for periods of 2 to 5 years.

Stewart[444] caused guinea-pigs to inhale asbestos dust. After 12 weeks, he found numerous asbestosis bodies in the alveoli and some in the alveolar walls. Some of the bodies were "beaded", in the process of degeneration, and they all gave an intense Prussian blue reaction, showing the presence of iron in the outer coating. Scattered, giant phagocytes in the alveoli contained asbestosis bodies. No fibrosis in the lungs or thickening of the alveolar walls was observed; the experiments lasted 20 weeks.

Large-scale animal studies were made during some 25 years in Gardner's laboratory at Saranac Lake. Vorwald, Durkan and Pratt[440] reviewed and summarized this work. When injected intravenously into rabbits, finely ground asbestos (chrysotile, amosite, crocidolite, anthophyllite and tremolite) produced only the reaction of an inert foreign body. There was no fibrosis of the liver, spleen or other organs as is observed when quartz is injected intravenously. When chrysotile (0·25 g or less) was injected intravenously 5 of 6 animals died, no reason for the deaths could be found.

Guinea-pigs inhaled asbestos for periods up to 33 months. The dust collected about the respiratory bronchioles, where fibrosis developed; the peripheral alveoli were not involved. A segregation of the fibrous and non-fibrous particles was observed, only the latter being transported to the lymph nodes. Asbestosis bodies were formed in 2 months. A cellular reaction was first observed about one year after the first exposure to the dust and a delicate fibrosis appeared after a further 4 months. The fibrosis progressed thereafter and, as the collagen fibres contracted, alveoli were partially closed and distorted. The appearance of the tissue resembled that of an adenoma; similar structures have been described in the lungs of guinea-pigs which had inhaled silicon carbide.[445]

When administered to guinea-pigs by intratracheal injection, chrysotile produced fibrosis. Two months after the dust was administered, there was well-marked cellular proliferation and focal

fibrosis about the respiratory bronchioles, asbestosis bodies were not observed After six months, asbestosis bodies were abundant in the lungs but, perhaps due to the contraction of the fibrous tissue, the reaction was less extensive Later, the fibrous tissue, localized around the terminal bronchioles, became hyalinized until, after 12 months, there were well-developed peribronchial and intra-bronchial adenomatoid areas of fibrosis

Species differences—Although Vorwald and his associates[440] obtained a definite fibrotic response to inhaled asbestos fibres in guinea-pigs, no fibrosis could be produced in rabbits As there were no fibres or asbestosis bodies in the lungs at autopsy, it was argued that the upper respiratory tract in these animals is an efficient filtration mechanism, adequate to exclude fibres from the lung

Well-marked peribronchiolar fibrosis has been observed in rats following the inhalation of long fibre asbestos dust but hardly any asbestosis bodies were present, in mice numerous asbestosis bodies were observed but no fibrosis Some cellular connective tissue forms a sheath around bronchioles in the lungs of cats following the inhalation of asbestos fibres, but typical asbestosis bodies are not produced The location of the lesions is similar to that found in guinea-pigs but the lesions develop much more slowly

Fibre length—Vorwald and his associates[440] compared the fibro-genic activity of asbestos dust of short fibre length ($3\ \mu$) with that of samples containing much longer fibres (20–$50\ \mu$) The dust was administered to guinea-pigs both by inhalation and by intratracheal injection

Guinea-pigs kept in an atmosphere containing long chrysotile fibres developed lesions consisting of cellular connective tissue about the terminal bronchioles after 8 months The adjacent parenchyma was affected after 16 months Lesions were large enough to be seen macroscopically after 20 months

By contrast when the guinea-pigs inhaled chrysotile fibres which were mainly shorter than $3\ \mu$ they showed but little reaction to the dust, only scattered phagocytes and an occasional minute asbestosis body were observed Cellular accumulations about terminal bronchioles were visible microscopically after 2 years, but no abnormality was sufficiently gross to be detected with a hand lens There was a slight increase in reticular tissue, but no true fibrosis in the tracheobronchial nodes after 30 months

Chrysotile fibres in the size range 20–$50\ \mu$ are evidently pathogenic The conclusion that particles less than $3\ \mu$ long are relatively harmless must be drawn with some reservations because of the experimental difficulties encountered in the tests Vorwald showed that strictly comparable dusty atmospheres containing asbestos of different

fibre lengths could not be produced: The average values (Table 12 2), which are taken from the detailed control analyses of the atmospheres,

are supported by those obtained by intratracheal injection. Long

fibrosis after 12 months When the administered dust particles were below 3 μ in size, they evoked an initial proliferative reaction

TABLE 12.2

Differential Counts (percentage of total count)

	Non-fibrous particles			Fibrous particles		Clumps	Analysis	
	< 3 μ	3–10 μ	>10μ	>10 μ	< 10 μ	Clumps	Chrysotile (per cent)	Serpentine (per cent)
Long fibre	65 4	1 1	0	25 8	1 0	1 0	60	20
Short fibre (ball milled)	90 6	4 8	0	0 8	0 6	3 2	15	60

and the dust became localized about the bronchioles but after 12

particles which are smaller than the critical size are removed by macrophages whilst those above this size do not reach the distal air spaces

King and others[446] obtained rather different results when asbestos of graded fibre length was transferred to the lungs of rabbits by

Effects of different types of asbestos and other fibrous particles.-Vorwald and others[440] found that inhaled serpentine, of particle size less than 3 μ, when injected intratracheally induced simple phagocytosis in the lungs of guinea-pigs but that it had produced no fibrosis 1 year after the experiment commenced.

When administered by intratracheal injection (dose 50 mg) the fibrous minerals chrysotile (Thetford and Arizona), amosite, croci-

dolite (Bolivia and S Africa) and tremolite all produced fibrosis about the bronchioles Brucite, MgO H_2O, produced a similar reaction In all cases asbestosis bodies were formed but often they were not observed until after the fibrosis was well established Sundius and Bygden[431] found that "asbestosis" bodies formed around rutile needles

Anthophyllite, another fibrous mineral of the amphibole group produced no fibrosis After 1 month scattered intrabronchiolar dust foci were observed but after 8 months there was little evidence of dust Lymphocytic infiltration of the bronchiolar walls, giant cells, and a few atypical asbestosis bodies were seen after a month No explanation of the inert character of this asbestos has been offered

Glass wool was also inert Giant cells collected the particles which could be seen as fine spicules in the cytoplasm and formed clumps in the peripheral air spaces No fibrosis was visible after a year

Progress of lesions after discontinuance of dust exposure—Guinea-pigs were exposed to an atmosphere containing asbestos dust for periods of 6 or 9 months, then kept in a normal atmosphere for periods up to 3 years The initial cellular reaction to the dust was replaced by thin strands of fibrous tissue 8 to 11 months after exposure ceased As the fibres matured they contracted so that the amount of scar tissue decreased with time Experimental asbestosis does not, then progress after the animal is removed from the dust laden atmosphere

Relation between asbestosis and tuberculosis—When guinea pigs which had inhaled asbestos dust for 26 months were transferred to a normal atmosphere and then infected with tubercle bacilli the course of the tuberculosis was not appreciably altered When the infection was coincident with the onset of the exposure to dust the results were variable in some animals the disease did not progress but in most there was a temporary progression and subsequent healing There is no evidence that asbestos dust significantly affects the course of a tuberculous infection

Aetiology

Two theories have been used to explain the damage caused to the lung by asbestos The one theory,[440, 431, 423] which is supported largely by the results of animal experiments suggests that the damage is purely mechanical—that it is due to the fibrous nature of the dust The following evidence supports this view Only asbestos fibres which are more than 20 μ and less than 50 μ long have been found to cause fibrosis in the lungs of animals[440] Moreover fibrosis has been produced in the lungs of guinea pigs by the intratracheal injection of brucite fibres, which contain less than 1 per cent SiO_2

On the other hand fibres of glass wool do not cause fibrosis. To explain this it has been suggested that the fibres do not initiate fibrosis unless they are very flexible. Glass fibres are much less flexible than chrysotile fibres—but so are brucite fibres. If chrysotile fibres are ignited, their structure is changed and water is lost. No fibrosis is produced when the ignited material is injected in guinea-pigs. It has been emphasized that fibrosis has been produced by asbestos fibres only in the lung and the peritoneum These are regions in which there is constant movement In the liver, spleen and subcutaneous tissue no fibrosis has been produced by asbestos

The chemical theory of asbestosis regards the disease as a special form of [illegible]
layer of [illegible]
the bod[illegible]
leaving [illegible]
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[illegible]

subsequent stages which lead to the development of lesions are similar to those found in silicosis

There is ample confirmation that fibrosis can be produced in the lungs of guinea-pigs by intratracheally-injected or inhaled asbestos fibres. The results of many of these experiments and those in which non-siliceous fibrous dusts were administered to animals support the view that the tissue damage in asbestosis is caused mechanically. The theory of mechanical damage is based mainly on the results of the animal experiments carried out in the Saranac laboratory and it assumes that the effects observed in animals are identical with those found in cases of human asbestosis Knox tabulated the following differences.

Experimental Asbestosis	*Human Asbestosis*
1 Has a short incubation period Fibrosis observed within one month of injection of fibres, contrast more than 2 months for quartz powder	1. Has a long incubation period of several years.
2 Condition regressed on cessation of exposure to dust	2 Has not been observed to regress; there is evidence of progression
3 No characteristic X-ray changes.	3. Definite X-ray changes when sufficiently established
4 Heart enlargement is not found	4. Heart enlargement and later degeneration are often found
5. Asbestosis bodies are produced early and the changes which occur in old bodies are not related to the degree of fibrosis	5 Changes are found in the asbestosis bodies which are related to the degree of fibrosis In well established cases there is "ageing" of bodies and clumping of bodies.

6 Sometimes there is nodular fibrosis	6 Nodular fibrosis is rarely, if ever, found
7 Produced by a non-silicate mineral fibre	7 No record of its production by fibres other than asbestos
8 Few fibres present in relation to the degree of fibrosis	8 Many fibres present in relation to the degree of fibrosis

There are other anomalies Thus, whilst the formation of asbestosis bodies is considered to be a defence mechanism of the body, Vorwald, Durkan and Pratt[440] found that the degree of fibrosis produced by asbestos was greatest in man (++) and that the asbestosis bodies were most numerous. In the fibrosed (2+) guinea-pigs' lungs "moderately" numerous bodies were observed, whilst in the rabbit, cat, rat, mouse and dog minimal (+) or no fibrosis was produced and asbestosis bodies were rare Both Gardner and King expressed the opinion that only the early stages of asbestosis have been reproduced in animals, the later stages have still to be demonstrated

The studies made by Knox and Beattie[428] on the human lungs which had been exposed to asbestos dust suggest that the damage may be chemical, due to (presumably) silicic acid which is liberated when the asbestosis bodies disintegrate They found large numbers of small particles when the asbestosis was advanced They concluded "Our findings thus indicate that a rise in the numbers of small mineral particles derived presumably from the breakdown of asbestosis bodies is associated with severe fibrotic changes in the lung parenchyma This implies that either these particles or some other product of the breakdown of the bodies can exert a fibrogenic effect on lung tissue If these products are removed as rapidly as they are formed, then either no asbestosis develops or a minimal degree of change occurs It is suggested that a reduced rate of removal of these products may be due to partial blockage of the drainage routes from the lung, i e, either towards the lung hilus or towards the pleural surface It is conceivable that any pathological process which would cause any inflammatory change in the hilum or in the lymph nodes into which the pleural lymphatics drain might cause a further reduction in the drainage rate and might precipitate the onset of severe fibrotic changes Cardiac decompensation too might be a factor in the precipitation of these changes "

Beger[438] and Champeix and Boutevílle[439] from optical and electron microscopic observations concluded that the action of asbestos was chemical and that asbestosis was an indirect silicosis Fowweather[447] analysed lungs from persons who had died of asbestosis and compared the mineral content with that of lungs which had not been unduly exposed to siliceous dust He found that, if the analytical figures

for the normal lungs were subtracted from those from the asbestosis cases, the extra mineral matter appeared to be only silica He concluded · "One cannot avoid the conclusion that the asbestos has undergone decomposition in the lung, with deposition of SiO_2" and he suggested that the disease is "due to the chemical action of silica . liberated in situ from inhaled silicates capable of relatively easy decomposition within the lungs".

Asbestosis and cancer of the lung

Statistics have been published which suggest that the incidence of cancer of the lung is higher among asbestos workers than among the general population Merewether stated in the Report of H M Chief Inspector of Factories,[448] that carcinoma of the lung was
(13 per cent) *but in 91 of*
from personal
21 (14 per cent)
6 (6 9 per cent)
asized that it is
nificant because
f women to men
workers in industries in which asbestos is handled is much higher than in the industries in which silica is used and amongst the general population. Lung cancer is more common amongst men than women. These facts give the figures an added significance. If only the male subjects who contracted asbestosis are considered, the incidence of carcinoma of the lung is 17 per cent in the group studied by Merewether and 20 per cent in that studied by Gloyne. A comparison of the incidence in different industrial groups of carcinoma of the lung associated with pneumoconiosis is made in the chart (Fig 12.7)

Doll[449] studied the records of a group of 105 persons who had died after working in the asbestos industry. Of these, 18 had lung cancer and in 15 cases the cancer was associated with asbestosis He compared the mortality in a group of 113 men who had worked for 20 *years or more in the industry* with that in a corresponding group of the general population. Thirty-nine deaths occurred in the one *group whereas the expected number* was 15·4. The excess was due to lung cancer, and other respiratory and cardiovascular diseases He stated "*From the data it can be concluded* that lung cancer was hazard of certain asbestos workers and that the

He pointed out, however, *that the*
in the industry before the pathogenic nature of the dust was recog-

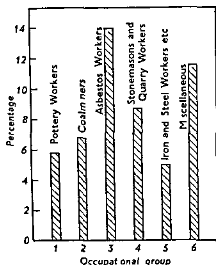


Fig 12 7 Mal gnant neoplasms asso ciated with pneumoconios s (After Gloyne *Lancet* **260** 810 1951)

nized and before the introduction of the Asbestos Industry Regula tions 1931 which controlled the conditions in asbestosis factories

Whilst most investigators believe that a relationship is probable between asbestosis and carcinoma of the lung [450 697] others[153 288] do not Experiments with animals have shown negative or inconclusive results [451 452 453 454] See also Rombola [636]

CHAPTER 13

COAL-MINERS' PNEUMOCONIOSIS

History of the disease in England

The earliest document in which coal-mining in England is mentioned is "The Saxon Chronicle of Peterborough", written in 852 Meiklejohn[455] has outlined the history of coal-mining in this country since that date and has given a detailed account of the history of lung diseases in the industry. Blackening of the lungs, then called melanosis, and associated diseases were observed during the nineteenth century. "Phthisis with melanosis is frequently of long duration and commonly, for a considerable time, does not shew any alarming symptom. All persons affected with this species of phthisis have attained an advanced age, rarely less than 50 years. When the disease is quite single they do not suffer much in the chest" (Bayle, 1815) Laennec[456] distinguished between true melanosis, a form of cancer, and the blackening which is due to the inhalation of dust and aerosols. It was Gregory[457] in 1831 who related the pulmonary condition found in coal-miners to their occupation and he described the condition of the lungs of a soldier who had been employed for 10 or 12 years as a collier "with a view of calling the attention of these practitioners who reside in the vicinity of the great coal-mines, and who may have charge of the health of miners, to the existence of a disease, to which that numerous class of the community would appear to be peculiarly exposed". Gregory asked whether the inhalation of the coal dust "had led ultimately to disorganization of the pulmonary tissue? in like manner as one form of phthisis is found to be particularly prevalent among those who by their occupations are most exposed to the inhalation of small irritating particles, such as stone-cutters, millers and needle-grinders"

Craig[458] in 1834 evolved a technique for examining the distribution of the dust in the lungs of deceased miners He inflated the lung, dried it, then sectioned it in various directions. The air cells in the sections were distinctly visible with the unaided eye or under low-power magnification He carefully described the emphysema which is recognized as a characteristic of coal-miners' pneumoconiosis:

"The air cells are greatly dilated throughout its whole substance Instead of being of their natural size, which is a little larger than a pin's point, they are generally of the size of a pea Some are as large as to admit the point of the little finger In some parts the cells, besides being simply dilated, are ruptured into one another, and present cavities varying from the size of a hazel nut to that of a walnut"

Stratton[459] in 1838 used the word "anthracosis" to describe the condition of the lung which is induced by colliery dusts As this word was also used to describe the blackening of the lungs caused by other dusts, "coal-miners' pneumoconiosis" is a better term

By studying the writings of the earlier clinicians Meiklejohn has shown that pneumoconiosis was widespread among coal-miners at the beginning of the nineteenth century but that it had become very rare by the end of the century During the twentieth century pneumoconiosis again became a serious menace in the coalfields of Great Britain A number of factors were operative Increased mechanization, particularly the use of mechanical picks and coalcutters, raised the dust level of the mine air enormously, the easily won coal having been mined, the workings became deeper and ventilation more difficult, much thinner coal seams had to be worked and consequently more dust was produced from the clod above and below the coal

A striking feature of the incidence of pneumoconiosis in the coalfields was the preponderance of cases in South Wales In 1935, 449 certificates of death or disablement due to silicosis were issued to miners, of which 398 were in respect of South Wales colliers In 1938 of 434 certificates issued 382 related to men in the South Wales collieries and 205 of these to men in the anthracite field The anthracite coalfield which represented one-fiftieth of the output of British coalfields claimed half the silicosis victims In England, 1,135 coal-workers were awarded compensation for pneumoconiosis under the Workmen's Compensation Acts during the two years 1950, 1951

Browne[460] has suggested that the difference between the incidence of pneumoconiosis in South Wales and that in other areas is not due to any difference in conditions or in the nature of the coal or rocks but rather to the age at which the miners started to work underground In the Welsh coalfields it used to be customary for workers to be sent underground at the age of 12 but in other areas youths were not employed at the coal face until they were older If allowance is made for the difference in the age at which the miners commenced work at the coal-face, the incidence of pneumoconiosis appears to be the same in two such diverse areas as Rhondda Fach and

Durham. Charts which illustrate this are shown in Figs. 13.1 and 13.2.

In 1937 the Pulmonary Diseases Committee of the Medical Research Council, at the request of the Home Office and the Mines Department, began an investigation into pneumoconiosis in the South Wales coalfields. Their findings were presented in three reports between 1942 and 1945.

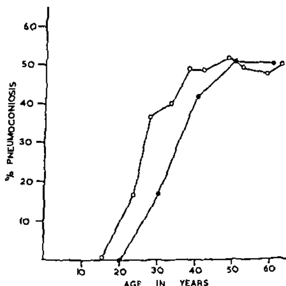


Fig 13 1 Incidence of pneumoconiosis at different ages in four Durham collieries (●) and four collieries in the Rhondda Fach (○)

The composition and concentration of the air-borne dust

The dust which a coal-miner breathes is complex. Besides the dust arising from the disintegration of coal, which itself is always

production of pneumoconiosis has been debated

The mineral matter in the ash of dust collected from several South Wales collieries was shown by X-ray diffraction and by chemical analysis to contain members of the kaolin and mica groups and, usually, quartz. Other materials, such as carbonates (calcite and ankerite-dolomite), sulphates and sulphides, were also identified.

Different ashes contained from 1 to 20 per cent of quartz There was 0 1 to 4 7 per cent quartz in the dust and 2 to 16 per cent total silica The kaolin and carbonate were considered to be derived mainly from the mineral matter of the coal seam, and the mica (illite) and quartz from the associated rocks (roof, clod, floor, etc) The extraneous mineral matter associated with the coal was found to contain quartz when the samples were from high incidence mines

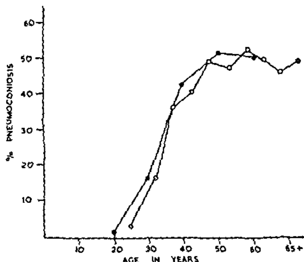


Fig 13 2 The graph which represents the incidence of pneumoconiosis in the Durham collieries has been moved 10 years to the left to allow for the difference in the age at which the boys commenced work underground The two graphs are now almost coincident

(Figs 13 1 and 13 2 are reproduced with permission from a paper by Prof C R Browne, *Brit J industr Med* **12** 279 1955)

but quartz was absent when they were from the low-incidence mines[507] The incidence of pulmonary abnormalities in the miners is significantly and positively correlated with the average ash concentration of the dust in the air of these South Wales pits This is illustrated in Fig 13 3[527]

In tissue from the lungs of coal miners there was practically no dust below 0 1 μ[455] Most of the particles below 2 μ (64 per cent) were between 0 1 μ and 0 5 μ

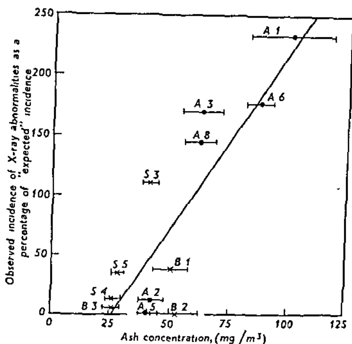


Fig 13 3 Relation between incidence of X-ray abnormalities and the ash concentration in certain South Wales collieries

The points (● in anthracite pits, × in steam coal and bitu-

Description of coal-miners' pneumoconiosis

At post-mortem, the characteristic feature of the sectioned diseased lung of a coal-miner is a generalized blackening[260]; there are black consolidated areas and between these the tissue may be *oedematous* or there may be areas of spongy emphysema In the most advanced cases, particularly when the miner has worked in hard headings, very little aerated lung tissue remains, the consolidated areas extending over the entire substance, except for small regions in the lower lung The lung is black or grey according to whether the worker had spells at the coal face or worked entirely in hard headings Some *lungs* retain considerable amounts of coal dust yet may be regarded as

almost normal Cavitation may occur even in the absence of tuberculosis and this may be the effect of stone-dust [451]

Examined microscopically, sections of a diseased lung show alveoli which are crowded with monocytes, the cytoplasm of which is packed with dust Cells of similar appearance are observed also in the lymphatic channels and in the lymph nodes at the root of the lungs Coronas of dust-laden cells next form around the blood vessels and the bronchioles The alveolar walls become distended with dust cells and the consequent blockage of the lymph vessels arrests the movement of the newly arriving phagocytes

The prolonged inhalation of "coal" dust results in the formation of small patches of altered tissue throughout the lung These take the form of blackened spots up to 5 mm diameter which, if they contain much fibrous tissue, are hard to the touch In some cases these dust foci may remain soft and unchanged for many years but in other cases fibrosis develops early, fine reticulin fibres being replaced by coarse tougher, collagen fibres A later stage is marked by the formation of fibrous nodules The main process by which dust foci increase is that of the accumulation of phagocytes in adjacent alveoli and alveolar walls Subsequently there is interalveolar fibrosis [412]

The air-spaces in and around the soft dust foci are dilated and the tissue has throughout a honeycomb appearance, but the centres of the hard nodules are solid, although they too are surrounded by a honeycomb structure due to the emphysema The focal emphysema is a dilatation of the respiratory bronchioles around which the dust has accumulated[281] (Fig 13 4), and it is mainly evident in the well-developed lesions The second order bronchioles are usually surrounded by the most dust and show the greatest dilatation, the maximum diameter of the air passages may be quadrupled The dilatation of the bronchioles results later in the compression of the atria and the alveolar sacs

disappeared The black consolidated areas of the lung which are visible macroscopically consist entirely of nodules between which are collections of dust cells

fibrotic nodules, similar to those in the lung, surrounded by dust-laden cells. In the nodules the lymphoid tissue disappears, but there may be normal areas which are almost devoid of dust between the nodules.



Fig 13 4. Focal dust lesion in a collier showing the relationship of the dust to the air-passages, which extend from a terminal bronchiole to the alveolar sacs

Respiratory bronchioles 1–3 show mild dilatation, i e. mild focal emphysema Desquamated epithelium and dust cells lie free in the lumen at one point Haematoxylin and eosin, ×10 (Heppleston, *J Path and Bact*, 66, 235, 1953)

Cummins[432] stressed the progressive nature of the disease: ". . this pneumoconiosis of coal-miners is a progressive condition, ... through a con-

to a condition of dyspnoea and breathlessness which makes work impossible". The simple pneumoconiosis of coal-workers seldom

causes cardiac failure although the right heart is frequently enlarged [641] It usually manifests itself by dyspnoea which is brought about by the following sequence [281] The dilatation of the respiratory bronchioles is equivalent to an increase in the dead space of the

sible for much of the disablement of the uncomplicated pneumoconiosis [641]

Belt and Ferris[610] differentiated between a primary lesion dust reticulation and a later condition nodular reticulation in the progressive effect of coal mine dusts on the lung in the collieries of South Wales Dust reticulation is a diffuse pigmentation of the framework of the lung accompanied by a fairly uniform increase of reticulin fibres Others[260 643] describe the early lesions not as diffuse but as characteristically focal

This latter view is held by Heppleston[281] who examined a number of early cases from South Wales He described localized collections

lymphoid tissue Del cate reticular fibres run through these foci

fibrous tissue In normal respiration contraction of the muscle in the bronchioles is the main process of inspiration The consolidated tissue narrows and shortens the air passages and expands the vesicular tissue the atria and alveolar sacs are reduced but the alveoli are increased in size When dust consolidation prevents the expansion of the vesicular tissue the muscular force is transmitted to the respiratory bronchioles When the accumulations of dust have

produced atrophy of the bronchiolar muscle, the normal shortening and constriction of the respiratory bronchioles does not occur. The result is dilatation of the respiratory bronchioles, that is, focal emphysema. Focal emphysema is found only when muscular atrophy has occurred.

Gough's method of cutting sections from a complete lung and mounting them on paper has proved invaluable in the study of emphysema. From a comparison of these sections with X-radiographs he has concluded that simple postero-anterior radiographs are [illegible] a in [illegible] ken [illegible] al.

Superimposed infection

[illegible]

cent had associated tuberculosis. Again, Sokoloff[359] in 1936 found that more than half of 418 American coal-miners had tuberculosis The coal dust is also said to produce in the miner a predisposition to pneumonia.[311] Gooding observed that tuberculosis is often modified when it accompanies coal-miners' pneumoconiosis and is often overlooked. Indeed the apparent absence of tuberculosis in coal-miners has led to the suggestion that coal dust protects the lungs against tuberculosis This was believed during the last century: "It is in the highest degree probable that coal dust possesses the property of hindering the development of tuberculosis, and of arresting its progress" (Hirst,[460] 1871) This same suggestion has been made repeatedly since then; for example Mavrogordato[608] stated "It is well known that colliers do not now develop miners' phthisis"; and Haldane[609]. "the dust they breathe protects them from serious dangers" Gardner[308] believed that the incidence of tuberculosis is high among the Welsh miners, and Belt and Ferris[610] suggested that tuberculosis occurred frequently among coal-miners but that it is difficult to recognize and is often overlooked. This view is supported by most recent clinical and pathological studies.[611, 612, 613, 614, 615]

James[461] considered that for the development of massive fibrosis in coal-miners two factors are necessary; they are dust and tuberculosis He described massive dust foci in the lungs of men without massive disease In eleven men who developed the disease rapidly, nine definitely and the other two probably had tuberculosis. Martin[462] believed that coal-miners' pneumoconiosis bears no relation to silicosis. He studied miners in a soft coal area and found

usually only simple pneumoconiosis (disseminated small nodulation) by X-ray He stated that another factor besides dust, probably infection, is necessary for the production of massive fibrosis

King and his collaborators[605, 606, 607, 616] injected intratracheally into guinea-pigs several types of tubercle bacilli with and without admixed coal-mine dust Whilst the dust alone produced no lesions and the bacilli alone produced lesions which disappeared or at least regressed to small calcified nodules, the mixture of dust and bacilli produced extensive tuberculous cavities or massive pulmonary fibrosis The dusts used were artificially prepared and contained about 20 per cent of siliceous matter, mostly mica, quartz and kaolin Earlier, Cummins[611] had shown that anthracite dust and dead tubercle bacilli would produce larger lesions in the lungs of animals than would either the dust or the bacilli alone Zaidi *et al* [606] found that coal-mine dust did not stimulate the growth of strain 3073 tubercle bacilli *in vitro*

When coal-miners' pneumoconiosis is complicated by infection, areas of massive fibrosis, which include large infected nodules,[463] are superimposed on the general picture of multiple, small nodules These infected areas occur particularly in the upper half of the lung, the infected tissue being black and hard, and there may be areas of liquefaction which contain a black fluid The nodules may be up to 1 cm in diameter They are solid, showing less emphysema than is characteristic of non-infected nodules The pleura is thick and the lungs may adhere to the chest wall Gooding[641] estimated that about half the silicotic coal-miners die from heart failure and half from accompanying infection Men with pneumoconiosis who show evidence of associated tuberculosis become disabled earlier than uncomplicated cases

Simple coal-miners' pneumoconiosis presents an X-ray picture of reticulation due to the superimposition of the shadows of dust foci It is sometimes difficult to detect It has been stated[464] that the radiographic changes can be detected before much harm has been done and removal of the worker from further exposure can prevent the progressive massive fibrosis which causes serious disability Meiklejohn,[465] however is less sure of this and he has emphasized that the diagnosis of early pneumoconiosis in coal-miners is more difficult than the diagnosis of silicosis There is rarely doubt about the diagnosis when infection has resulted in a degree of massive fibrosis

Serum Proteins in Coal-miners' pneumoconiosis

Prignot[585,651] studying 91 coalminers with pneumoconiosis, found the total blood proteins only slightly altered by the disease The

serum albumin values were reduced and the serum globulin values increased. There were, however, wide variations.

Carbon and mineral dust-fractions

It has been stated[451, 280] that coal dust alone cannot cause fibrosis but only pigmentation, which has no influence on pulmonary function In the lungs of hundreds of Ruhr coal-miners which were examined post mortem, fibrosis was absent except when rock dust had been inhaled in quantity [423] The black material found in the lungs has been definitely identified as coal Silica- and iron-containing particles have also been identified in the cytoplasm of phagocytes.[280] There is no considerable accumulation of coal dust, however, unless there is a preceding fibrotic condition caused by silica. In the absence of fibrosis, coal dust is rapidly eliminated.

It is widely believed that the black lung of coal-miners is due primarily to silicosis[466, 467] which prevents the elimination of coal dust The diseased lungs may contain ten to twenty times as much silica as normal lungs. Indeed, it has been stated[468] that the lung fibrosis in the coal-miners of South Wales resembles that found in the gold miners on the Rand who have silicosis and that the silica content of the lung ash is approximately the same in both cases The importance of the mineral fraction of the dust in coal-mines has been stressed by King and Hart.[469] On the other hand Hollmann[470] believed that pure carbon can cause pneumoconiosis He described pneumoconiosis in workers handling carbon which contained only 1 per cent of ash Three cases of pneumoconiosis in workers on coke screens have been reported.[471]

Although the incidence of pneumoconiosis is far higher in the anthracite-producing areas of South Wales than in the areas producing soft coal, no difference could be found between the effects of dust from a colliery producing bituminous coal and that from a colliery producing anthracite on the fibrosing action of quartz.[365] Mixtures of the dust with quartz were administered to rats by intratracheal injection Comparison of the resulting lesions with those produced by quartz alone suggested that the mine dusts had no modifying action

Coal-miners' pneumoconiosis and cancer of the lung

Gooding[641] found no evidence of an increased incidence of primary lung cancer in men who had suffered from coal-miners' pneumoconiosis

CHAPTER 14

THE EFFECTS OF OTHER SILICEOUS DUSTS

Kaolin, Talc, Mica, Slate, Felspar, Sillimanite, Cement, Carborundum

There is no doubt that, when inhaled, pure silica can produce a severe pneumoconiosis. It is less certain how far silicates other than asbestos can produce a pneumoconiosis which is comparable with silicosis. Silica occurs very widely in mineral deposits and most silicate mineral dusts are contaminated with the dust of silica. When a pneumoconiosis is produced, it is often questionable whether the disease is due to the silicate or to the smaller concentration of free silica.

Animal experiments with pure silicate powders are often difficult to interpret because the silicates, if they do produce a pneumoconiosis, act much more slowly than, for example, quartz. If an attempt is made to accelerate the action of the dust by administering very high concentrations some tissue damage usually results. It is probable that, when inhaled in very high concentrations, any dust can produce damage to the lung tissue. Beattie[472] was able to produce fibrosis "with more or less obliteration of the lung tissue" by causing guinea-pigs to inhale large amounts of many types of dust, e.g. granite, carborundum, cement, limestone and dust from a tin mine, a lead mine and a pottery. These very high concentrations of dust are not normally encountered in industry, however. This type of response to high concentrations of dust, a response which is largely independent of the nature of the dust has been given the name "benign pneumo-coniosis" [473]. The evidence for and against the existence of a pneumoconiosis due to a number of silicate dusts will be outlined.

Kaolin

Kaolin (china clay) is used in the ceramic industry, as a filler in paper, and as a weighting material in textiles. In England most of the high-quality kaolin is mined in Cornwall. It is believed there that kaolin dust does not produce harmful effects when inhaled.[474] On the other hand, some authors have suggested that kaolin can produce a pneumoconiosis.[475]

When kaolin from South Wales was administered to rats by intratracheal injection, it produced neither fibrosis nor emphysema[475] Cornish kaolin gave essentially similar results It produced only a mild reticulin reaction which was not comparable with that produced by quartz

Middleton[474] showed that X-radiographs of the lungs of a worker in the Cornish c [illegible] lung fields. Ha [illegible] [illegible] graphs of several workers. Shadows on an X-ray film may be due to aggregations of any opaque bodies and do not necessarily indicate fibrosis. These workers show few, if any, symptoms and certainly the dust of pure kaolin does not produce serious disability.[473]

Silicosis occurs among workers in the bone china industry[477] Bone china is made from Cornish stone, china clay and calcined bone; it does not contain added free silica. It is possible, but not certain, that the disease has been caused by the flint dust which was used as a parting powder before it was replaced by alumina, and by flint dust from earthenware departments which usually contaminates the air of the entire pottery works.

Talc

A pneumoconiosis due to talc was first described by Thorel[478] in 1896 Recently, the occurrence of the disease has been described in workers in a number of industries Alivisatos, Pontikakis and Terzis[479] quoted twenty-five papers which had appeared on talc pneumoconiosis during the last 25 years

From a study of the literature up to 1950,[480] it was concluded that the disease caused by talc was a separate entity. It was called "talcosis" The radiological pictures resemble those of asbestosis. The initial symptoms observed are a cough, the sputum containing grey talc bodies, with dyspnoea of exertion Radiographs show numerous nodular shadows which are sometimes confluent. Later the radiographs show a tumour-like appearance.

Twenty-eight factory workers employed preparing cosmetic and medical talc were examined[481] and 3 of these were found to have pneumoconiosis; one who had worked 19 years had a pneumoconiosis at stage I, 2 who had worked 25 and 30 years respectively at stage II McLaughlin[482] described 2 cases He found that, although the factory dust was mainly composed of flakes of talc with a few fibres, there were more fibres than flakes in the lung The fibres were up to 10 μ in length and about 5 μ wide He concluded "without doubt the fibrosis in the lungs was associated with the presence of the particles of talc dust".

An account has been given of pneumoconiosis due to the inhalation

of talc which has developed rapidly [479] Seven cases of talcosis developed after the persons had been exposed to high concentrations of talc dust for from 16 to 24 months Particle counts on konimeter samples taken in a number of places in the mill indicated atmospheric dust concentrations of from 550 to 2 000 particles per c c of air Particles of free silica were absent

Massive asymmetrical fibrosis in a worker in the rubber industry has been described [609] The talc dust inhaled contained only a very small amount of free silica Talc pneumoconiosis in the textile industry has also been described [652]

Experiments in which talc was administered to animals did not produce gross fibrosis When talc is injected in saline suspension into guinea pigs, the talc becomes surrounded by a thin layer of fibrous tissue which is only sufficient to isolate the powder The talcs used in these animal experiments [482] contained carbonates and serpentine It was noticed that the carbonate disappeared some time after the injection and that, if much carbonate was present, the serpentine disappeared also When the injected material contained 52 per cent talc and 39 per cent serpentine, there was little change in its composition, even 15 months after injection

Mica

Mica is used mainly as a thermal and electrical insulator but also in the manufacture of paper and paint It is mined in India where it occurs with free silica, drillings from the Bihar mines showed from 11 to 67 per cent of free silica [484] In these mines there is a high incidence of silicosis

Radiographs of workers who had been exposed to mica dust showed diffuse shadows in the lung suggesting fibrosis [474] On this evidence it has been suggested that mica dust itself can produce pulmonary fibrosis (See also ref 345)

Slate

Slate is composed mainly of mica and quartz The amount of free silica in the material may vary considerably, examples of published figures are free silica 7 per cent [485] and 15 per cent [486] Because of the dust arising from adjacent mineral layers the proportion of free silica in the dust of slate mines and quarries may be much higher than in slate itself Hanstein [487] found 35 per cent free silica in the dust taken from a slate mine

There are many reports of pneumoconiosis in workers who handle slate Some reports indicate that the effects are slight [485, 488] but others suggest that slate dust may produce a severe pneumoconiosis [489, 490, 491] The difference between the reports is probably

accounted for by the wide variations in the silica content of the dusts from different sources Canepa[653] described silico-tuberculosis and nodular silicosis in three slate workers. The nodules in the lungs were large. The slate contained free silica (10–15 per cent), calcium carbonate (40–50 per cent) and silicates (37–43 per cent).

The fibrosis seen in the lungs of workers in slate mines and quarries may be partly diffuse and partly nodular [492] The lymph glands may be hard and enlarged to several times their normal size.

When administered to rats by intratracheal injection, slate dust ... d quartz dust, produced far ... to be due to the quartz content of the slate.

Felspar

Felspar is used in the glass and pottery industries, in making vitreous enamels and in electrical porcelains. Commercial felspars may contain up to 20 per cent of free quartz The early experiments of Gardner suggested that felspar did not cause fibrosis and, indeed, to some extent countered the fibrogenic properties of silica When Gardner injected felspar dust intravenously into rabbits or intraperitoneally into guinea-pigs he found no fibrosis.[493, 494]

Mohanty, Roberts, King and Harrison injected felspar dust intratracheally[486] into the lungs of rats. The felspar produced very little fibrosis even after 17 months In a parallel experiment, *quartz controls had fibrosis in the lungs after 4 months* Few animal experiments have been made with felspar dust but such results as have been obtained indicate that felspar dust is relatively harmless See also Chargy, Castelain and Gerard[654]

Pumice

Pumice is a silicate glass of volcanic origin. The dust contains about 1 8 per cent free silica. Four cases of pumice pneumoconiosis were described by Ferrara a ... 20–30 years, linear fibrosis, ... tion" and massive fibrosi ... emphysema were absent ... gically the disease was considered to resemble silicosis.

Sillimanite

Sillimanite is an aluminium silicate. It occurs in masses of long crystals which do not break down into fibres as does asbestos but shatter into a powder. It is used as a refractory and in the manufacture of porcelain. Middleton[474] examined radiographs of the chests of 15 men who had handled sillimanite. He found ab-

normalities in the lungs of only 4, and suggested that the dust was not highly dangerous

Animal experiments, in which rabbits were exposed to sillimanite dust for two hours daily, produced fibrosis in the lungs of some animals [495] Animals which survived for two years had well defined dust nodules in the lungs This suggests that sillimanite is not altogether harmless

Cement

The literature describing the effects of cement dust on the lung tissue is confusing Most observers consider it to be one of the least harmful of dusts [496, 497, 498, 488, 500, 501] Landis[4] described cement as harmless Thompson, Brindaye, Russell and Bloomfield[502] said that "workers in cement factories never suffered from silicosis"

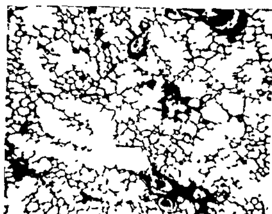
No hazard due to the inhalation of cement dust was found by workers from the Saranac Laboratory [503] They based their conclusion on an examination of 2,278 workers in the industry and also concluded that the incidence of lung infections was lower than that of the general population Other observers found localized sclerosis in the lungs of 6 cement workers [504] Another report stated that there is rather more respiratory disease in cement workers than in workers in most other industries Vyskocil[351] found that exposure to cement dust aggravated bronchitis and produced emphysema, older workers being most affected

In a study of the cement industry made by the U S Public Health Service,[505] 15 men were found to have pneumoconiosis among a group of 37, all of whom had been in the industry more than 3 years The diagnosis was made on X-ray findings, clinical symptoms were absent Russell[506] also stated that there was more disability due to respiratory causes in the cement industry than in relatively non-dusty industries

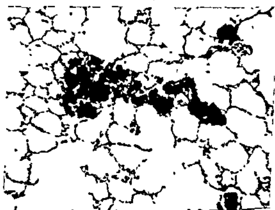
A possible explanation of these confusing results may lie in the variable compositions of the materials handled at different stages in the manufacture of cement The composition of cement is given as CaO 62 per cent, SiO_2 22 per cent The proportion of free silica varies however, it is only about 1 per cent in the finished product but may be anything up to 6 5 per cent in the material handled in the crusher house, raw mill and stone house It must also be remembered that shadows on the radiographs do not necessarily imply that there is fibrosis in the lung, the dust itself may give shadows

Doerr[22] reported what he believed to be the first recorded case of severe pneumoconiosis attributable to the inhalation of cement dust Radiographs first revealed nodular shadows and later massive sha

in the lung fields At necropsy, massive fibrosis was found in both lungs. There was no tuberculosis. A chemical analysis of the lungs was revealing The ash contained 50 per cent silica and only 4 per cent calcium; the dust *in the air of the works contained 40 per*



(A)



(B)

Fig 14 1 Photomicrograph of a section of the lung of a rat which had inhaled silicon carbide dust.

The dust is collected into a few isolated areas and no damage to the tissues is apparent (Reticulin stain, *A* × 60, *B* × 200)

cent calcium Moreover quartz was found in the lung by X-ray diffraction methods Doerr thought that the quartz may have been formed by decomposition of the silicate in the lung; silicic acid might be so produced but not quartz

Silicon Carbide and Carborundum

Carborundum is a silicon carbide manufactured by The Carborundum Company Limited All the published evidence appears to show that silicon carbide dust is harmless[508, 470] or can produce only a mild pneumoconiosis Bruusgard[509] has described a pneumoconiosis in workers using carborundum and Smith and Perina[510] found that workers preparing synthetic abrasive wheels (mixed silicon carbide and synthetic alumina) may contract a mild pneumoconiosis They found[511] 7 cases showing nodular fibrosis among 53 workers but 4 of these had also inhaled other significant dusts These authors suggested that carborundum gave free silica under the action of the tissue fluids Others[512] observed no pneumoconiosis in workers who inhaled silicon carbide dust although their radiographs may show a fine reticular structure and perhaps minute nodules

Experiments in which silicon carbide dust was administered to animals by inhalation or injection technique indicate that this material is remarkably inert Gardner[513] reported that the material produced practically no reaction The masses of particles lie inert in the tissue for years without producing more than a strictly localized non progressive chronic inflammation of slight degree Rats which have inhaled high concentrations of silicon carbide dust in an experimental dust tunnel in the author s laboratory have shown very little fibrosis in the lungs although the lymph glands were fibrosed (Fig 14 I)

CHAPTER 15

THE EFFECTS OF SOME NON-SILICEOUS DUSTS

BERYLLIUM, ALUMINIUM, IRON OXIDE, GRAPHITE, CALCIUM CARBONATE AND SULPHATE, TUNGSTEN CARBIDE, TIN OXIDE, BARITE, ZIRCON, TITANIUM OXIDE, CALCIUM FLUORIDE AND ORGANIC MATERIALS

Beryllium

Beryllium is used in alloys (beryllium-copper, beryllium-nickel, beryllium-aluminium) Pure beryllium rods are necessary for

reported in 1933 Both acute and chronic forms of berylliosis have been described. One observer[515] examined 98 cases of acute and 48 cases of chronic pulmonary berylliosis in 13 years

Acute toxicity.—The acute disease is a chemical pneumonitis which occurs whilst the person is still working. It starts with a cough. In a few days dyspnoea is apparent on exertion and later whilst at rest. Death may occur within two weeks The morbid anatomy of the lungs resembles that of a chemical pneumonitis caused by other substances although there is less necrosis A

ity. A

/m³

A fluorescent grade ic, but only to higher animals, at 90 mg /m³ concentration The only weight Two other

spectively, were non-

400°C contained a different form of beryllia from the others; it had a lower refractive index and was singly refractive The particles in the other grades were mainly birefringent

Chronic berylliosis —Up to 6 years may elapse between the last exposure to beryllium dust and the appearance of chronic berylliosis.

The symptoms start with vague ill-health, it may be weeks or months before abnormal signs appear in the lungs There is extreme dyspnoea About one third of the patients die and about one third are permanently disabled The rest recover

The lungs of a person with chronic berylliosis show gross emphysema and they have scattered, fine nodules and diffuse interstitial fibrosis Granulomata form within the alveolar spaces by organization of the exudate They have a fibrinoid centre with peripheral fibrosis

Early X-radiographs of the lungs show a diffuse, finely granular appearance which is homogeneously distributed Later, fine nodulation is superimposed on this picture Confluence of nodules occurs but much less commonly than in silicosis Beryllium is excreted in the urine The concentrations found varied from 0 1 to 2 micrograms per litre, the values being highest in acute berylliosis but beryllium may be excreted by persons who have been exposed to beryllium but are not suffering from berylliosis, so this test is not

of significant exposure to beryllium dust and beryllium must be detected in the urine Differentiation from some other lung diseases such as nodular silicosis, siderosis or chronic miliary tuberculosis may be difficult There is no doubt about the individuality of the disease, however Van Ordstrand stated ' Chronic berylliosis shows no pathologic similarity to any other recognized occupational disease "

The effects of beryllia dust on the lungs of rats has been studied [519] A reaction is produced in the lungs within 7 days The dust becomes engulfed in phagocytes which congregate and produce some fibrosis but granulomatous lesions do not occur, and there is no response comparable with chronic pulmonary berylliosis in man Policard[520] has made histological studies of the effects of beryllia on animal tissues Others[521] studied the fate of beryllium compounds in the rat

Eisenbud s advisory committee of the United States Atomic Energy Commission in 1949 gave the following maximum concentration values

1 average in-plant atmospheric concentration of beryllium should not exceed 2 micrograms per cubic metre during an 8 hour day,
2 average monthly concentration near the plant should not exceed 0 01 micrograms per cubic metre

3 no worker should be exposed to a concentration greater than 25 micrograms per cubic metre at any time

In one large American company the recovery of beryllium in the ventilation system has more than offset the cost of precautions.

Aluminium and aluminium oxide

Fine dust formed from aluminium is usually covered with a film of aluminium oxide; when aluminium powder is formed by stamping, the aluminium particles are covered with stearin or paraffin Brull[595] described the effects of the dust on 22 workmen in Canada, of whom 6 died The symptoms were observed after 2 to 10 years' exposure. In German factories where aluminium powder was made by the stamp process, *many workers were affected by a severe* pneumoconiosis.[523, 524, 525, 526] Radiographs of these men showed a [illegible] who died [illegible] dust-laden [illegible]s only 3 months after commencement of work. In another works where aluminium was smelted 97 workers were examined of whom 18 *had* heavy damage to the lung [528]

Aluminosis has been described[527] as an interstitial non-nodular lung fibrosis There is often considerable emphysema. In many of the cases described the inhaled air contained high concentrations of both alumina and silica.

Animal experiments with aluminium dust are contradictory. One worker[529] reported that the lungs of rabbits which had inhaled aluminium dust rarely showed more than a foreign body reaction, although diffuse fibrosis of the lung develops, similar to that seen in workers exposed to aluminium dust, when the inhalation of the aluminium was combined with a pneumococcal infection. Others[530] produced in animals a similar picture to that observed in humans.

King and others[625] found that, injected intratracheally, large doses of both hydrated alumina and aluminium phosphate produced reticulin nodules in the lungs of rats and that the nodules induced by alumina developed into dense collagenous fibrosis The *condensed fume from a corundum furnace*, consisting of about equal amounts of silica and alumina, produced a less severe fibrosis, although an acute exudative reaction to the dust sometimes *killed* the rats in a few days The dust slowly disappears from the lung King emphasized that his results were obtained with very large doses of dust and that consequently they have no bearing on the therapeutic use of *aluminium* *The effect of* duralumin dust on the lungs of rats has been described.[626]

A possible explanation of the different results obtained by different observers may lie in the variations of the surface coating on the material. The particles may be coated with an aluminium oxide layer or an organic liquid, stearin or paraffin, which prevents surface oxidation. Jager and Jager[531] pointed out that aluminium metal readily reacts with sodium chloride to give sodium aluminate and aluminium chloride which hydrolyze to aluminium hydroxide. It is an interesting point that aluminium hydroxide can polymerize to giant molecules as does silicic acid and it can react with proteins.

Twenty-five cases of pneumoconiosis in men employed at the smelting ovens where pure calcined alumina is processed to give corundum were examined by Hagen[532]. Eleven of these men died with silicosis. Radiographs of the chests of these men differed from those of men with silicosis. The shadows showed a fine fibrotic network throughout the lungs. The corundum dust contained 99.3 per cent Al_2O_3 so there could be little doubt that the alumina itself was the pathogenic agent.

Pulmonary disease has also been described in workers who produced corundum from bauxite. Analyses of the dust in this plant showed it to consist of bauxite with 29 to 44 per cent silica. The disease was originally attributed to aluminium oxide but was later thought to be caused by silica. (For a summary of papers see Gartner[533].)

It seems to be well established that under some conditions, aluminium oxide can produce a severe pneumoconiosis. On the other hand, several thousand workers in the mining, ceramic and foundry industries who were treated therapeutically with aluminium dust showed no ill effects attributable to the metal[529], and grinders who were making duralumin propellers and who inhaled an atmosphere containing 1 mg of aluminium particles per cubic metre in the size range 2–7 μ appeared to be in good health and did not appear to be suffering from pneumoconiosis[534]. Alumina has replaced flint for the placing of the clay ware for biscuit firing in the manufacture of English bone china and no evidence of pneumoconiosis in workers using this material has been found[535]. Again, the Industrial Pulmonary Diseases Committee of the Medical Research Council found no evidence of pneumoconiosis caused by aluminium oxide in 50 workers at the British Aluminium Company[536]. The dust concentrations to which the men were exposed varied from about 500 to 2,500 particles per c.c., the median size being 0.23–0.5 μ.

Iron oxide (siderosis)

Iron oxide dust is inhaled by workers in several industries. Iron oxide is mined as haematite, ferric oxide is used as a polishing powder

and ferric oxide dust and fumes arise in the welding and grinding of steel

In haematite mines particularly in the north west of England pneumoconiosis was detected in some of the workers. The Committee on Industrial Pulmonary Disease of the Medical Research Council issued a report in 1933 with the following conclusions:

1 A certain proportion of haematite miners suffer from a form of pneumoconiosis caused by the inhalation of mine dust containing both finely-divided haematite and silica There appears to be a notable pre-disposition to the development of tuberculosis, and in some cases the disease causes disablement and death.
2. The disease presents definite characteristics, so that it can be recognized on clinical and radiological grounds during life and by post-mortem examination of the lungs in fatal cases
3 There was not sufficient evidence to
say what part

2 micronodules producing a filoreticular, granite-like picture, and
3 irregularly distributed nodules

The sputum contains iron-packed macrophages Mignolet[543] never found nodulation due to iron oxide in welders but only localized or generalized sclerosis

Radiographs of the lungs of workers employed in polishing silver articles with rouge showed opacities similar to those found in radiographs of welders' lungs [544] The lungs of one worker were examined at post-mortem They were emphysematous but showed no fibrotic changes due to the dust Hollmann[470] considers that iron oxide dust is harmless

A condition resembling siderosis has been induced in rats by the intratracheal injection of ferric oxide [545] No fibrosis was found in the lungs of these animals

The abnormal radiographs of lungs which have been exposed to iron oxide are believed to be due solely to the radio-opacity of the dust The condition is not serious and there are *no* clinical symptoms except for slight coughing

Graphite

Graphite is a natural crystalline form of carbon It is mined in many parts of the world It is usually very impure and on combustion may yield up to 30 per cent or more of ash which is mainly silica

Dunner[546] described abnormalities in the radiographs of the chests of workers who had inhaled graphite Dunner and Bagnall[547] described cavitation due to necrosis in the lungs of a man who had worked with graphite for 17 years and was treated for tuberculosis X-radiographs revealed massive opacities in the lungs About 6 years after he left the industry, the man coughed up a mass of black material containing carbon particles mostly smaller than 5 µ No silica was detected No tubercle bacilli were found in the sputum

Parmeggiani[548] described a mild pneumoconiosis in the graphite miners of the Chisone Valley of the Piedmont, Italy The condition is detected by abnormalities in the chest radiographs but clinically it produces no disturbance except some dyspnoea of effort It is rarely accompanied by pulmonary tuberculosis The dust in these workings contained fine particles of which 91 to 99 per cent were between 0 2–5 µ in diameter Analysis of the material showed that it contained 56 per cent carbon and 25 per cent silica including 11 per cent of free silica Parmeggiani suggested that the condition was due to silica, it being a mixed pneumoconiosis in which graphite tends to *prevent* the fibrosing action of the silica

While it seems likely that the pneumoconiosis produced by graphite is due to the siliceous material it contains,[473] observations on 547 workers who were exposed to heavy concentrations of carbon dust (less than 1 per cent ash and containing no free silica) showed that a few were suffering from disease which resembled silicosis in every way [508] Hollmann[470] reported that 25 men of a group of 90 who had been exposed to carbon dust for long periods had pneumoconiosis. This carbon had an ash of less than 1 per cent.

A case of pneumoconiosis in a worker who handled synthetic graphite and carborundum has been described.[549] Silicosis was diagnosed and at post-mortem much collagenous fibrosis was found No quartz was detected either in the lung or in the atmosphere of the works. Intraperitoneal injections of carborundum and graphite were found to produce fibrosis in animals. Carborundum itself is not believed to cause a serious pneumoconiosis.

Limestone (calcium carbonate) and gypsum (calcium sulphate)

When it was recognized, centuries ago, that dusts could produce diseases of the lung, it was believed that limestone dust was not incriminated (Chapter 1). That belief is still held today: "there is every reason to believe that limestone and gypsum dusts are harmless if free from silica".[550] Limestone[551] may cause a slight pulmonary reaction but this is not associated with progressive fibrosis Com- [illegible] Real, Griffin [illegible] quartz in [illegible] [551] found 0·7 to 2 9 per cent free silica in quarried limestone. When limestone and gypsum are used for stone-dusting in coal-mines, analytical control is indicated or the use of the material may involve a silicosis risk Doig[627] found pneumoconiosis in several limestone workers but stated that the disease was due to the free silica associated with the limestone. The dust contained from 2 to 10 per cent of free silica.

Comparing the health of stonemasons in Holland, Kranenberg[553] found that of 16 who had worked sandstone for 20 to 30 years, 5 had serious silicosis There were no comparable cases of silicosis in a group of 74 masons who had worked limestone during a similar period of time, although 5 were slightly affected. Stonemasons who worked with both sandstone and limestone or marble were less affected than those who worked with sandstone alone No pneumoconiosis was found in 14 men who had worked in limestone for 12 to 35 years although the concentration of dust particles in the size range 0 5–5 μ was many thousands of particles per c c.[628]

Tungsten carbide

A pneumoconiosis in workers in the tungsten carbide tool industry has been described[554] From histological studies on rats it was deduced that the tungsten carbide itself was probably not the causative agent Cobalt also present was suspect

Tin oxide

Cases of pneumoconiosis due to the inhalation of tin oxide have been reported[555 556 557 558] in the workers who packed the oxide into bags or smelted tin Severe X ray changes are observed There is but little disablement and only slight dyspnoea

Barite ($BaSO_4$)

Camba[559] could find no X ray evidence of any pneumoconiosis caused by barium sulphate dust

Zircon

Zircon $ZrSiO_4$ appears to be a singularly inert substance When injected into rats no pathological effects were observed[560]

Titanium oxide

Titanium oxide is used as a pigment Guinea pigs exposed to titanium oxide dust became affected[561] The pathology of the lungs resembled that found in other types of pneumoconiosis The name of titanosis was suggested for the disease

Calcium fluoride

Animals injected intraperitoneally with natural fluorspar and with synthetic calcium fluoride of high purity showed a fibrotic response more intense than that produced by quartz[562] Dust from fluorspar has long been known to produce silicosis but as the fluorspar occurs naturally with quartz it was uncertain which mineral produced the effect

Organic materials

A number of organic dusts can produce lung diseases Perry[473] has given an account of these and has listed relevant references Byssinosis caused by the inhalation of cotton dust is an asthmatic condition and is not classified as a pneumoconiosis Agricultural workers are liable to contract a lung disease farmer s lung caused by dusts arising from hay straw and grain[563] It is possible that the active agents are fungi The patient has dyspnoea and

a cough. X-radiographs show changes in the lung, first a fine reticulation, then a snow-flake mottling with, later, an increase in density of the mottling and an increase in the hilar and perihilar shadows. The radiographs finally show patches of increased density due to the coalescence of areas of fibrosis There is considerable emphysema and the lung sections show bands of fibrous *tissue traversing the lung substance.*

The dust of bagasse, extracted sugar cane which is used for making fibre-board, may cause a disease which resembles "farmer's lung".

A pneumoconiosis due to cork dust has been described.[656]

CHAPTER 16

PROTECTIVE MEASURES AGAINST PNEUMOCONIOSIS

Pneumoconiosis cannot be cured. Most investigators regard it as a progressive disease the lesions continuing to develop after exposure to the dust has ceased [564, 565] although some [546] believe that simple pneumoconiosis uncomplicated by infection is not progressive but that the condition remains more or less static after a delay period of about 2 years if the person is removed from further exposure to dust. As the course of the disease cannot be altered the methods of combating pneumoconiosis must aim at prevention.

The principal methods used against pneumoconiosis are the removal of dust by efficient ventilation the suppression of dust by water sprays etc and the use of respirators. Certain therapeutic methods such as the inhalation of aluminium dust have been tried but are not in general use.

Dust control in mines

The methods of dust control that can be used in mines differ in some respects from those which are used in factories. As a rule dust must be removed by the general ventilation local exhaust is impracticable. The ventilation of mines presents difficult problems. The air must be carried for long distances from the surface to the working places and care must be taken to ensure that dust is not carried from one working place to another. In spite of precautions dust concentrations may rise to high levels. In one French coal mine for example where the ventilation was reported to be very good dust concentrations in the working places of 6 to 500 mg/m^3 were found [566].

In metal mines dust is formed mainly in drilling holes for blasting shovelling and loading the ore and muck and in timbering. At the surface dry crushing also produces a lot of dust. In coal mines cutting especially machine cutting produces a great deal of dust. Shearing centre cutting overcutting and undercutting all produce very high concentrations. Dust is also formed in blasting shovelling and drilling [567].

Dust control is probably more efficient in the South African mines

than anywhere else in the world Government regulations which apply there insist that blasting may be carried out only when the men are out of the mine and that an adequate time must be allowed before the men return. Holes may be drilled in the rock only by drills in which water is forced down the centre of the shaft; every mine must have running water delivered through a pipe not less than one inch in diameter at a pressure of 30 lb./in.^{2} within 50 ft. of the working place.

Very efficient ventilating systems are used in the South African mines. The air which is pumped to the working places is often first cooled. Water sprays are used to increase the rate of settlement of the dust particles and the ground is wetted-down before and after blasting. A summary of these methods has been published.[568]

In the Kolar Gold Field of India the temperature of the rock is very high (140°F) and it is impossible to use water to prevent dust formation as the resultant high wet-bulb temperature would make work impossible [569] Drilling is carried out with hollow drills through which air is blown to remove the dust from the drill holes.

In the Kolar mines the main method of dust control must be by ventilation. Because of the high temperature, large volumes of air were pumped to the face even before the silicosis hazard was recognized Cooled air is taken through the main shafts and haulage drives to the main development areas Some of it returns from there to ventilate the stopes. In some cases the stopes are ventilated with splits off the main down-cast.

A great deal of thought has gone into the designing of apparatus for reducing [illegible] Hoods have been designed which surro[illegible] he dust to be sucked away as it i[illegible] steam[574] have been used in an attempt to lay the dust. Because of practical difficulties none of these methods has been generally adopted In coal-mines dust has been effectively suppressed in drilling by using hollow drills through which air is drawn, then passed through a filter. By using special steel, the diameter of the central hole may be increased to as much as ½-inch and an adequate through-put of air is thus ensured

Dust control in workshops and factories

In foundries, silica dust reaches the atmosphere mainly during the conditioning and conveying of the sand, and in shaking-out and cleaning the castings [575] Improvement in the condition of the air can often be made by isolating these operations so that the dust from one [illegible] part of the shop where another operation [illegible] ventilating hoods [illegible] the dust The

design and placing of hoods is discussed in a later section The importance of segregating dusty operations is emphasized in the Acts of Parliament which apply to factories such as the regulations applicable to Iron and Steel Foundries (Chapter 17)

In some trades dust is quite needlessly blown into the air For example most operations in the working of granite and sandstone produce silica dust It is often workshop practice to blow away by a blast of air dust which accumulates on the surface of the work thus producing a high concentration of dust in the air Suction is of course preferable Where siliceous stone is worked the best shops use local exhaust ventilation and for some operations the workers wear masks

Sometimes it has been found possible to replace siliceous materials by other materials which do not produce pneumoconiosis The erious mortality amongst workers in the china biscuit factories anufacturing English bone china was due to the inhalation of dust om the fine flint used in the placing of the clay Alumina was substituted for flint[575] with beneficial results In parts of Norway sand is no longer used for casting but olivine (essentially forsterite Mg_2SiO_4) is used in its place[576, 577] Where the use of sand in parting powders has been discontinued in English foundries a corresponding decrease in the incidence of pneumoconiosis has been observed[578] Again white cements were manufactured which contained calcined flint Because of the silicosis risk involved in the use of the flint some manufacturers now use substitute materials Often the cost of replacing silica by an inert material is prohibitive however

Early methods of ventilation

Mines were ventilated several thousand years ago The copper mines in central Europe were efficiently ventilated by lighting wood fires in the mine shaft[579] Pliny stated that ventilation could be improved by the diligent shaking of a cloth in shallow workings Pliny was quoted and the method was illustrated by Agricola Agricola realized the importance of mine ventilation and devoted a number of pages of his *De re metallica* to this subject He described several methods of ventilating mines Apparently it was usual to blow air to the miner exhaust ventilation was seldom employed

Agricola classified ventilating machines into three genera The first receives and diverts into the shaft the blowing of the wind One such apparatus made like a barrel is shown in Fig 16 1 The second is made with fans The fans wooden paddles tipped with goose feathers were rotated by windmills watermills or by man power The last named type is shown in Fig 16 2 Blowing

machines of the third genus . . . are made with bellows, for by its blasts the shafts and tunnels are not only furnished with air through conduits or pipes, but they can also be cleared by suction of their heavy and pestilential vapours.' A workman compressed the bellows by hand (Fig. 16.3) or "by treading with his feet, just as persons compress those bellows of the organs which give out varied and sweet sounds in churches".



Fig. 16 1 Ventilation of a mine by diverting the prevailing wind

A—Wooden barrels, *B*—Hoops, *C*—Blow-holes, *D*—Pipe, *E*—Table, *F*—Axle, *G*—Opening in the bottom of the barrel, *H*—Wing (Agricola *De Re Metallica*)

It is probable that workshops and factories were not artificially

passing into the open air and so to rarify the air in this

workshop shall always tend

stone so as to

e stones for the

dry grinding of cutlery are arranged on this plan [Fig. 16·4] with wonderful benefit to the health of the workman."

It is apparent, then, that some factories were ventilated by sucking the dust-laden air from the building through wooden ducts by the middle of the last century. But fundamentally the methods of ventilation were those of Agricola's day. The Royal Commission of 1862, appointed to inquire into the health of workers in metalliferous



[illegible] "[illegible] mine by means of a fan [illegible] driven by water power
A—Hollow drum, B—Its blow-hole, C—Axle with fans, D—Drum which is made of rundles, E—Lower axle, F—Its toothed wheel, G—Water wheel. (Agricola, *De Re Metallica*.)

mines, remarked of the ventilation methods then in use[17]: "It does seem surprising how little has been the progress of ideas in the adaptation of ventilating machinery. There have, however, been remarkable improvements in the mode of construction of the fan, and a better theory of its action has been propounded."

Ventilation: the dispersal of dust

In some cases the dispersal of dust can be reduced if the conditions are first studied. Dust particles which are in the respiratory size

range are dispersed mainly by air movement, although larger particles may be projected long distances by kinetic energy from fast-moving machinery. Thus, if a carborundum particle $\frac{1}{16}$ in. in diameter is thrown 100 ft. into the air from a wheel which is revolving at 10,000 ft./min., a 10-μ particle would travel only 1 in. Fast-moving machinery (fly-wheels, large pulleys and belts) does, however, produce considerable air movement and so causes dispersion of fine dust.



Fig. 16 3. Ventilation of a mine by bellows.
A—Tunnel, *B*—Pipe, *C*—Nozzle of double bellows (Agricola *De Re Metallica*)

In factories and workshops air movement is often produced by convexion currents over radiators and ovens, but their velocity is usually not more than 25–75 ft./min. Draughts from open windows may be more significant. In designing an industrial exhaust system, all these sources of air movement are studied and, where they create a disturbance sufficient to affect the dust concentration, they are eliminated. Window draughts can often be dealt with by fixing suitable baffles or in some cases windows may be permanently closed with advantage.

The vibration of machinery, particularly of large panels on

machines often keeps dust in suspension which otherwise might settle. The transfer of materials may be responsible for the production of large amounts of dust. When a powder is transferred from a bag or barrel the first puff of air may have a velocity of up to 250 ft/min.

Ventilation: the design and positioning of exhaust hoods

In designing hoods for local exhaust it is necessary first to measure the velocity of escape from the source of the dust. The exhaust must draw the air towards the hood at a velocity greater than the

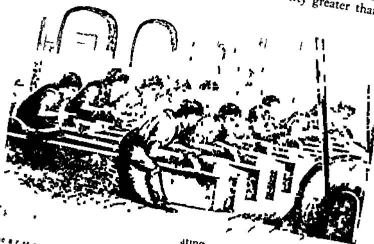


Fig. ... ating a workshop where cutlery was ground. The air streams induced by the rotating wheels were directed into ducts which led to the open air. (Tomlinson, *Illustrations of Useful Arts, Manufacture and Trades*, 1867.)

escape velocity. In most dust control a minimum exhaust air velocity of 75–100 ft/min is required; the usual value is about 500 ft/min. Studying the ventilation in a group of mines, Tebbens and Tattershaw[550] found that the dust concentration decreased logarithmically as the volume of ventilating air increased.

The hood is placed as near as possible to the source of the dust; the effectiveness of a hood decreases very rapidly as its distance from the dust source increases. Figs. 16.5 and 16.6 show contours representing the air velocities at different distances from a circular and a square opening. These contours show that at a distance from

the hood opening which is approximately equal to the diameter or width of the opening, the air velocity is reduced to ten per cent or less of its value at the mouth of the hood. Often a flange on an exhaust hood will increase its efficiency (Fig 16.7).

It is sometimes possible to almost completely enclose a machine or tool. Asbestos carding machines, for example, have been almost totally enclosed in some works. The dust extractor may be built in

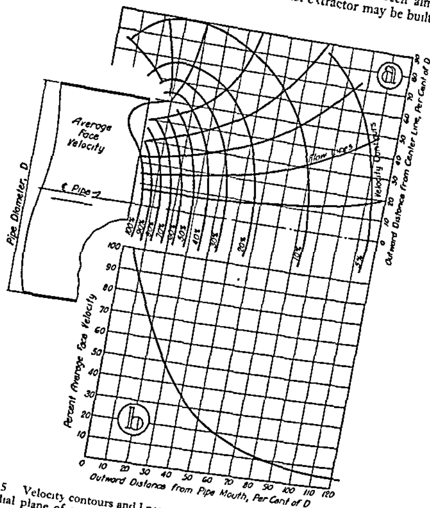


Fig. 16 5 Velocity contours and lines representing the direction of air-flow in a radial plane of a circular suction pipe (Alden *Design of Industrial Exhaust Systems*, Industrial Press, New York)

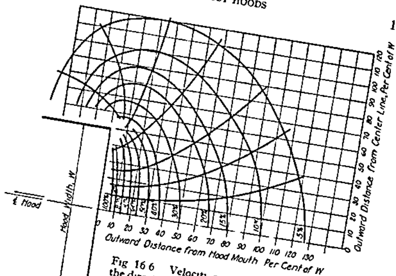


Fig 16 6 Velocity contours and lines representing the direction of air-flow in the centre line plane of a square suction hood (Alden *Design of Industrial Exhaust Systems* Industrial Press, New York)

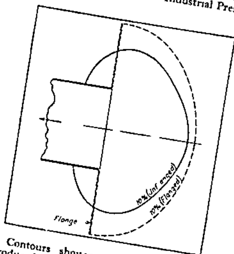


Fig 16 7 Contours showing the increased ventilating efficiency produced by fitting a flange to a ventilating duct (Alden *Design of Industrial Exhaust Systems* Industrial Press, New York)



a



b

Fig 16 8 Dustuctor cowl (a) with exhaust, (b) without exhaust.
(By courtesy of Holman Bros Ltd, Camborne)

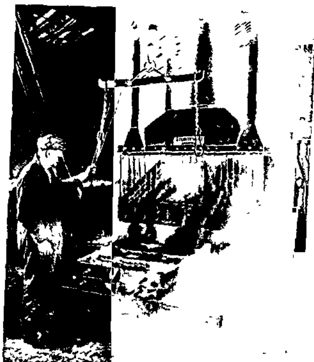


Fig 16 9 Exhaust system in the steel industry, side draught exhaust to a mechanical shake-out

Note the flanged hood placed to draw the dust which is shaken from the castings away from the operator The operator cannot pass between the shake-out and the exhaust hood (By courtesy of Sturtevant, London)

to some portable machines Fig 16 8 shows a portable surface grinder with a built-in cowl The one photograph shows the machine grinding a cast iron angle plate with its exhaust disconnected, the other shows the machine being used in the same way but with the extractor functioning The cloud of fine dust which is normally thrown into the air is now completely absent

Where dust is thrown from moving machinery, a hood is located so that the particles are thrown directly towards the hood, and the



Fig 16 10 Side draught exhaust at twin 6 ft × 4 ft vibratory shake-out at a foundry

Note how the exhaust removes the dust and fumes from the operator (By courtesy of Sturtevant London)

velocity of the air-flow towards the hood at the point of origin of the dust is made [illegible]

source of dust to take advantage of upward thermal currents In practice, side draughts are too powerful and the worker s head may be in the line of the draught Usually exhaust hoods are best

placed at the side of the source of dust Illustrations of hoods used for dust control in several processes in the iron and steel industry are shown in Figs 16.9, 16 10, 16.11, and 16 12. Larger hoods, which must sometimes be at some distance from the source of the dust, are erected in such a position that the operator can never come between the hood and the source of the dust.

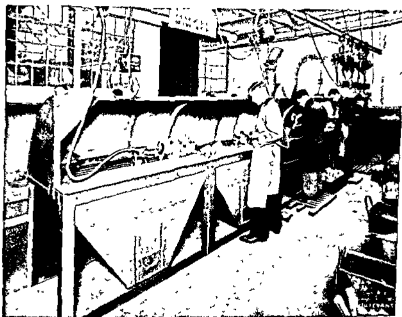


Fig 16 11 Exhaust system in the steel industry Installation at a fettling bench (by courtesy of Sturtevant, London)

General ventilation

Improvement in general ventilation is seldom sufficient in itself

often serves no useful purpose whatever.

Hoods used to improve the general ventilation are placed so that the natural air-flow in the workshop is towards the hood Provision is made for the entry of air, often the forced entry of air, in suitable parts of the building This is important. The object of the ventilating fan is not to attempt to produce a vacuum in the workshop but

to produce an air-flow which will carry the dust from the shop
Exhaust fans should not be placed so that they work in opposition
Ventilation ducts should be of adequate diameter A considerable loss in ventilating efficiency may result from the use of ducts which

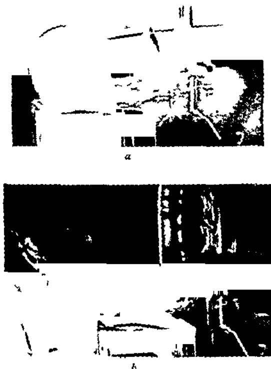


Fig 16 12 Dust clouds generated by a swing frame grinding machine (pig iron workpiece)

(a) Using a conventional machine (b) Using a machine incorporating the B C I R A integral exhaust system

[illegible]

one group of workers towards another

It is not usually practicable to clean and recirculate the air which has been removed from a workshop, since the efficient removal of dust from the air is a very expensive process. The values given in Table 16.1 show that most types of separators will not collect

TABLE 16.1

Approximate minimum particle size for which various separator types are suitable

Separator type	Minimum particle size, microns
Gravity	200
Inertial	50–150
Centrifugal	
Large-diameter cyclone	40–60
Small-diameter cyclone	20–30
Fan type	15–30
Filter	0.5
Scrubber	0.5–2.0
Electrical	0.001–1.0

particles in the lower pathological size range. A bag filter is usually very inefficient, particularly shortly after cleaning, since it relies on accumulated dust to trap other particles. Good fabric filters are somewhat more efficient. Wet washers are useless for cleaning air from small particles. The electrostatic precipitator and the venturi scrubber will remove nearly all (say 99 per cent) of the small particles from the exhaust air. The former is extremely costly to install; the latter, which injects high pressure water into a jet through which the air is passed, costs but little to instal but is very expensive in power. The cleaning and recirculation of the air is not, then, an economic proposition. Since the exhaust air cannot be freed from all dust, it [illegible] ensure that it does not [illegible] ts or chimneys of con- [illegible] ne engineers advocate [illegible] where it is diluted by, [illegible]

Water sprays

Many mines now use sprays to accelerate dust settlement, but if these are to work efficiently it is essential that the right type of spray equipment should be used and that the water should be fed to the

spray at high pressure.[581] Wetting agents increase the efficiency of sprays and less water is required. The value of water sprays is by no means generally admitted.[581, 583, 584] Some question whether the smallest dust particles are affected by the spray at all. From theoretical considerations it can be shown that the probability of a small dust particle colliding with a spray droplet is very small indeed and it is probably true that only the coarser particles, those outside the pathological size range, are affected. Others point out that, since minute droplets are inhaled and each droplet may contain up to 5,000 small particles, the spray may increase the dust hazard.

On the other hand, it has been claimed that water sprays in mines not only reduce the dust hazard but increase working efficiency by 10 per cent, mainly because visibility is improved.[585] A reduction in the dust content of mine air to one-ninth of the previous value by using wet methods has been claimed.[586] The value of wetting down surfaces has also been questioned. Settled dust may be prevented from rising, but the wet surfaces can have no effect on the fine suspended particles, which take many hours to settle.[582]

Perhaps the most successful method of dust suppression in coal mines involves the injection of water at high pressure through drill holes behind the coal face. By this procedure the coal measures are saturated and little dust is formed when the coal is worked and transported. A disadvantage of water-injection is that the roof is made less safe but this has been largely overcome by 'roof-stitching'. It is believed that water injection and dust removal through hollow drills will dramatically reduce the incidence of coal-miners' pneumoconiosis.

Respirators

Simple forms of respirators have been used as a protection against dangerous dusts for at least two thousand years. Pliny[586] described how pigs' bladders were used as dust masks. They were worn over the face so that the worker could see through the membrane although the nose was protected against direct dust. 'Persons polishing cinnabar in workshops tie on their face loose masks of bladder skin, to prevent their inhaling the dust in breathing, which is very pernicious, and nevertheless to allow them to see over the bladders.'

In more recent times cloth respirators were used. Agricola's work on mining methods, *De re metallica* has illustrations of men wearing clothing which covered part of the face as a protection against dust. Three centuries later Tomlinson[587] in his *Illustrations of Useful Arts, Manufactures and Trades* showed a needle-pointer wearing a piece of fabric tied around the face in the same manner to protect himself against dust from the grindstone (Fig. 16.13).

The factory regulations which cover some industries state that respirators must be provided. For example, the Iron and Steel Foundries Regulations, 1953, state that: "The occupier shall provide and maintain approved respirators for workers carrying out any operation creating a heavy dust concentration which cannot be dispelled quickly and effectively by the existing ventilation arrangements."



Fig 16 13 Needle-pointing by dry grinding
Note the cloth "respirator" worn by the operator (Tomlinson, *Illustrations of Useful Arts, Manufactures and Trades*, 1867)

Most of the respirators which were used before about 1940 were of little value against silicosis Either they did not remove the dust particles smaller than 5 μ which cause silicosis or if they did remove the finer particles, they were so resistant to the flow of air that workers could not wear them Recently much better respirators have been designed These use filter pads which have a large area but which are only a few millimetres thick They offer little resistance to the flow of air

The respirator which is most
in England is the Siebe, Gorma
designed at the suggestion of
Industrial Research, and is manufactured under licence from the Ministry of Labour and National Service. The Ministry makes periodical tests to ensure that the respirators are uniform in quality

and performance The respirator has a facepiece of flexible moulded rubber to which a filter unit of asbestos-wool mixture, covered with black fabric and quilted, is attached on either side Each filter consists of two pads separated by a spacing piece of corrugated perforated material The total filtering area of the respirator is approximately 54 in ² Each filter unit is provided with a non return inlet valve, a rubber disc on a metal seating to prevent exhaled, moisture-laden air from passing back through the filter



Fig 16 14 The Siebe Gorman Mark IV Dust Respirator

The filter units of the Mark IV, with their inlet valves, can be removed from the facepiece and replaced when they become clogged with dust

On the front of the respirator is a non return outlet valve so disposed as to cause condensed moisture, which may accumulate inside the facepiece, to be discharged when the wearer exhales The outlet valve is a rubber disc on a metal seating, and is protected by a perforated metal disc which prevents large particles from interfering with the closing of the valve For use in hot, moist atmospheres, the facepiece is embossed or "dimple marked" to prevent

the respirator from slipping on the face. Adjustable elastic straps hold the respirator in position on the face. This respirator weighs about 140 g. It removes 94 per cent of dust particles larger than 0.5 μ from the inhaled air.

Another type of respirator, the "Microfilter" (Fig. 16.15), was designed at the request of the Committee on Industrial Health of the British Steel Founders' Association

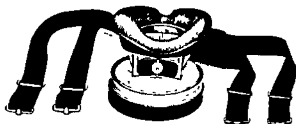


Fig. 16.15 The Siebe Gorman Microfilter Respirator

The "Microfilter" has a moulded plastic facepiece and filter holder to which is fitted a soft sponge-rubber face pad. The filter, a circular pad of Merino wool impregnated with resin, rests on a perforated metal platform and muslin diaphragm in the filter holder. It is held in place by a perforated metal plate and a screwed plastic cover.

The respirator is fitted with non-return inlet and outlet valves of low resistance. It is held in position on the face by four adjustable elastic bands. This respirator also bears the registered Certification Mark of the Ministry of Labour and National Service, and it is approved for use under the Asbestos Industry Regulations, 1931. Microfilter respirators with a positive air-feed have been described.[470]

The lethal particles of asbestos dust are believed to be those larger than about 5 μ. Even simpler types of respirators may be effective in trapping these particles. A loose pad of cotton wool held by a clip under the nose may be effective. The modern industrial dust respirator is light and easy to wear but it is quite impracticable for a person who is doing really heavy work to use any respirator except for short periods. Even if the person is engaged in light work a respirator becomes most uncomfortable if the temperature or the humidity is high.

Protective dusts

The possibility of using one dust to counteract the ill effects of another has been investigated This procedure was strongly advocated some thirty years ago, particularly by Haldane, who advocated the use of shale dust to counteract the effect of silica dust in mines Animal experiments have suggested that some dusts may give protection against silica but, applied industrially, the procedure has given rather unconvincing results Calcium sulphate[588] and sprays of calcium chloride solution have also been used

Considerable attention has been given to the use of aluminium dust as an antidote to silica Some description of the experimental work which led to its use was given in Chapters 5, 8 and 10 Many tests have been made on workers who regularly handle materials which give rise to silicosis, but the evidence is conflicting, whilst a number of reports[589 590 591 592 593] indicate that the inhalation of aluminium powder has a beneficial effect, retarding the symptoms of the disease, others[594 595 596] suggest that there is no evidence that aluminium is of therapeutic value

The aluminium powder which is used for inhalation therapy is specially prepared by the McIntyre Research Limited in America and Canada, it is stated to contain 95 per cent aluminium but aluminium oxidizes readily and analyses have shown that the material given therapeutically contains 80 per cent of aluminium oxide In the lung the material becomes aluminium hydroxide, Gardner and workers in the Saranac laboratory[597] preferred to administer aluminium hydroxide dust Because the particle size is below 5 μ, the aluminium powder is black The dust is administered by dispersing it into the air of the workers' changing room, or by allowing the men to inhale through mouthpieces leading from a chamber in which the dust is dispersed

The difficulty of assessing the value of aluminium therapy when applied to workmen, rather than to experimental animals is apparent and the evidence of its value is thought by some to be insufficient to justify its widespread adoption in industry An added complication is the discovery that aluminium itself can cause pneumoconiosis (Chapter 15) and the view has been expressed[598] that aluminium inhalation should not at present be recommended

Kennedy,[457] at the Medical Research Council's Treatment Centre, made observations on 120 carefully selected patients who had worked in the coalmining or pottery industry for at least ten years All the patients showed radiological evidence of pneumoconiosis but did not suffer from pulmonary tuberculosis or cardiovascular disease Some of these patients received metallic aluminium powder by

inhalation, some pure carbon with added metallic aluminium and some breathed only pure air. Treatment was continued for four years. Most of the patients, including those who received no aluminium, claimed symptomatic improvement but no improvement was shown in the radiological pictures or the tests of functional capacity. It was concluded that the symptomatic improvements were mainly psychological in origin and the Industrial Pulmonary Diseases Committee of the Medical Research Council considered that the treatment with aluminium "had no effect either on the symptoms or on the radiological progression of silicosis and pneumoconiosis. They do not recommend the adoption of this method of treatment" Note that these observations were made on patients with established lesions. There appears to be no evidence in humans which proves whether or not the *formation* of lesions is retarded if the aluminium is inhaled with the siliceous from the onset of the exposure Such a study would be more difficult but it would be more in accord with the animal experiments which have b...

Many objections have been ... dusts. It is difficult to f... ment and there is gener... , which may or may not be justified, against polluting a dusty atmosphere still further.

CHAPTER 17*

THE MEASUREMENT OF DUST CONCENTRATION

For the investigation and assessment of a dust hazard it is necessary to collect and evaluate suitable samples of the air borne dust. The complete examination of a dusty atmosphere involves the estimation both of the number of dust particles and the weight of dust in a unit volume of air. Samples large enough for chemical and petrological examination must also be collected.

It is questionable whether a dust hazard is better measured by the number or the mass of the pathogenic particles in the air. The [illegible]

collected for the determination of mass concentration are much more [illegible]

[illegible] a stated size from reaching the filter.

For the determination of particle count (number of dust particles in a cubic centimetre of air) several types of apparatus have been devised. The most accurate estimations are made with the thermal precipitator and this instrument is almost invariably used in fundamental research into dust problems. When a dusty atmosphere is to be examined solely from the aspect of dust control it is usually necessary only to have a means of comparing dust concentrations; the highest accuracy is unnecessary. The Konimeter, Owen's jet dust counter and the impinger are examples of instruments which are simpler in operation although less accurate than the thermal precipitator.

The mass concentration of dust (milligrams of dust in a cubic metre of air) is usually determined either by the salicylic acid filter or the naphthalene filter. Another instrument suitable for dust control, the Tyndallometer, measures the light which is scattered by

*This chapter is based on a series of papers written by the author and published in *Metallurgia* 1951.

suspended dust particles This instrument can give continuous recordings.

Other apparatus may be required for the collection of samples

pheres the salicylic acid filter may be used but where the dust concentration is very high, as in collieries and cement works, some type of cloth or paper filter will probably be preferred.



Fig 17 1. Diagram illustrating the dust-free space round a hot body

The thermal precipitator

This instrument gives accurate sampling of air-borne dust for microscopic observation. It was originally developed for the Department o
and Lomax.[59]
by Green and
Council, comp
sampling apparatus * The apparatus makes use of the fact that there is a dust-free space around a hot body, the magnitude of which depends on the temperature difference between the body and the surrounding air. Above the hot body, the space tapers off as a cone because of convexion currents (Fig 17.1)

The hot body in the thermal precipitator is an electrically heated wire placed between two microscope cover slips in such a position that the space between the wire and the cover-slips is entirely within the boundary of the dust free space When a measured volume of air is drawn through this space by means of an aspirator the dust which it carries is completely removed and adheres to the cover slips

Details of the thermal precipitator are shown in Fig 17 2 The head consists of two brass blocks which are held together by screws Between them are two thin sheets of bakelite cut to leave a channel running vertically across the head A resistance wire is stretched across the centre of the channel and is kept taut by a spring

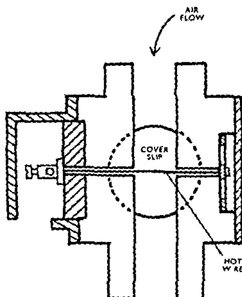


Fig 17 2 Thermal precipitator head

The microscope cover glasses (No 1 thickness ¾ in diameter) which take the samples are introduced through holes in the brass blocks They are placed either side of the heating wire on the thin bakelite strips where they are held by brass plugs kept in position by flat springs Electrical connection with the heating wire is made at one end to an insulated terminal and at the other to the brass

block of the head. The wire is heated by the current from a 2-volt accumulator which is maintained at 1·2 amps by adjusting a rheostat

The thermal precipitator head may be mounted on the water aspirator which is used for drawing the air sample through the apparatus. The aspirator has an outlet, from which water can be run out to give a regulated rate of flow of about 6 5 ml /min.

A thermal precipitator that gives continuous sampling has been designed At pre-set intervals the plugs to which the cover slips are attached are rotated so that sampling is continued along a fresh diameter In this way seven or eight samples may be obtained on one cover slip which represent the condition of the air during a complete working shift (Fig. 17.3)

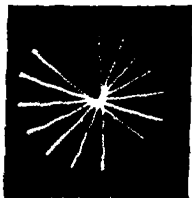


Fig 17 3 Multiple sample from automatic thermal precipitator.

Efficiency of the thermal precipitator —Tests made by Green and Watson have shown that the instrument collects almost 100 per cent of the dust particles in the air sampled This efficiency holds for particles up to at least 20 μ in diameter and for sampling rates up to 7 ml./min The lower size limit which can be counted is limited by the efficiency of the microscope. Under the oil immersion lens the smallest particles visible are between 0 1 and 0·2 μ in diameter, but by using a special attachment which takes a nitrocellulose film instead of a cover slip, it is possible to obtain thermal precipitator samples for examination under the electron microscope, when the lower size limit is reduced by about ten times

The konimeter

The thermal precipitator is cumbersome for taking large numbers of routine samples Of the several types of dust sampling apparatus which are available for routine observations but which do not give the absolute accuracy of the thermal precipitator the konimeter[39] has proved very popular in South Africa This instrument was developed over 45 years ago There are several designs but all work on the same principle that a measured volume of air is drawn

graticule

Konimeter samples are usually counted using dark ground illumina tion and under favourable conditions tests have shown that 50–60 per cent of particles are collected in dust clouds containing from 500 2 300 particles per c c The usual method of counting does not reveal particles smaller than 0 8 μ diameter Tests in the Wit watersrand Mines have shown that whereas determinations made with the konimeter gave values some 60 per cent of those obtained with the thermal precipitator or sedimentation cell when the number of particles was approximately 500 per ml this value dropped to only 30 per cent when the number of particles was 4 000 per ml

The highest efficiency is obtained if the konimeter is adjusted to avoid leakage if the jet adjustment and velocity of impingement are correct and if there is no contamination of the slide The microscope should be adjusted to secure maximum visibility of the smaller particles and all visible particles must be counted

Although the konimeter has considerable limitations it has proved a very valuable instrument in dust control Its absolute accuracy is not high but serial samples are comparable one with another and if proper precautions are taken its performance is consistent In most control work an absolute evaluation of the dustiness is not required it is necessary only to determine the relative dustiness of certain processes or the degree of reduction when for example new ventilation methods are tried

The jet dust counter

Another ingenious dust sampling apparatus described by Owens[598] in 1922 is the jet apparatus Fig 17 4 It resembles the konimeter in that a measured volume of the dust laden air is forced by means of a hand pump through a narrow slit so that it impinges on to a cover glass It differs from the konimeter in that the air

block of the head The wire is heated by the current from a 2-volt accumulator which is maintained at 1·2 amps by adjusting a rheostat

The thermal precipitator head may be mounted on the water aspirator which is used for drawing the air sample through the apparatus The aspirator has an outlet, from which water can be

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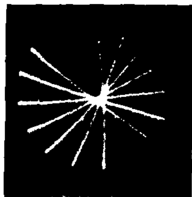


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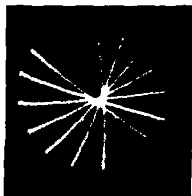
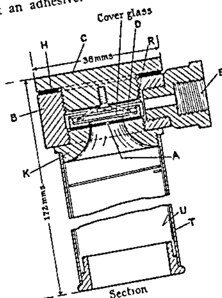


Fig. 17.3. Multiple sample from automatic thermal precipitator.

Efficiency of the thermal precipitator.—Tests made by Green and Watson have shown that the instrument collects almost 100 per cent of the dust particles in the air sampled. This efficiency holds for particles up to at least 20 μ in diameter and for sampling rates up to 7 ml./min. The lower size limit which can be counted is limited by the efficiency of the microscope. Under the oil immersion lens the smallest particles visible are between 0.1 and 0.2 μ in diameter, but by using a special attachment which takes a nitrocellulose film instead of a cover slip, it is possible to obtain thermal precipitator samples for examination under the electron microscope, when the lower size limit is reduced by about ten times.

passes through a damping chamber before reaching the slit so that it becomes saturated with moisture and the dust adheres to the glass surface without an adhesive. After passing through the slit, the



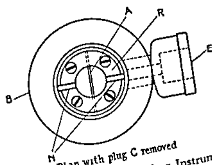


Fig 17 4 Owen's Jet Dust-sampling Instrument (*Proc. Roy Soc*, A 101, 18, 1922.)

A—Slot for forming jet, *B*—Brass sleeve, *C*—Plug, *D*—Spring washer, *E*—Connexion to hand pump, *H*—Washer, *K*—Brass piece with funnel-shaped hole, *T*—Brass tube lined with wet filter paper (*U*)

pressure of the air is suddenly reduced, its temperature drops and moisture condenses around the dust nuclei, these particles becoming attached to the glass plate. After the sample has been taken, the

slides; a size grading of the particles results This separation is an advantage since it facilitates counting To a large extent it prevents the coalescing of droplets when mists are sampled

The apparatus is hung from gallows by a light cord attached at its centre of gravity A wind vane is built on to the instrument so that it may always orientate itself to ensure that the direction of sampling is the same as the direction of the wind When sampling from still air, an orifice adaptor is used, otherwise very irregular deposits are obtained on the first slide

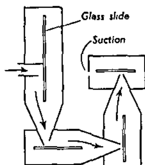


Fig 17 6 Diagrammatic representation of the cascade impactor showing the jet positions

As a source of suction for the cascade impactor it is convenient to use a small motor-driven pump or, better still an injector unit of a type designed to operate on compressed air from a bottle One such type of injector will provide a flow of 20 litres min through the apparatus for an expenditure of about 4 litres min of compressed air The rate of flow through the impactor is best controlled by fitting a critical pressure orifice

The measurement of the mass concentration of dust

Most of the earlier investigators did not attempt to count the number of particles collected from a known volume of air, but employed apparatus which was designed to obtain a sample that

number of particles present on the size distribution among the particles, *and on the density of the material from which the dust is*

Its efficiency increases with the sampling velocity, which is normally about 28 litres/min. Drinker gave its efficiency as 96 per cent on a silica dust cloud, but Green and Watson found the efficiency much lower It is usual practice to count impinger samples under low-power magnification (×200), which means that particles smaller than 0·8 μ are missed Using this technique, the efficiency of the impinger was found to be about 40 per cent The use of dark ground illumination can extend visibility to the lower particle sizes but it has been stated that the counts are then less reliable.

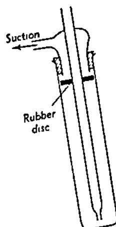


Fig 17 5 The impinger.

The cascade impactor

An apparatus which has been developed by the Ministry of Supply is known as the cascade impactor (Ministry of Supply Patent No. 580705) It was originally designed to sample mist droplets in the size range of 0 5–200 μ carried by wind of velocity around 8 m p h. It has since been applied to the sampling of all types of aerosols, including dust, and has also been adapted to sample from stationary air

The principle of the cascade impactor, Fig 17 6, is similar to that of the konimeter in that the sample is collected by forcing the air through a narrow jet to impinge on a glass slide coated with a suitable adhesive, but in the impactor the air must pass consecutively through four jets, each smaller than the last. As the air passes through a coarser jet its velocity is less than when it passes a finer jet and, because of this, finer particles are not retained by the earlier coated

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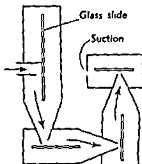


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The measurement of the mass concentration of dust

Most of the earlier investigators did not attempt to count the number of particles collected from a known volume of air, but employed apparatus which was designed to obtain a sample that could be weighed The particle count and mass concentration may give different pictures of a dust cloud and ideally, both values should be obtained The mass of dust in a volume of air depends on the number of particles present on the size distribution among the particles, and on the density of the material from which the dust is

made When a dust cloud contains mainly coarse, solid particles, the mass concentration relative to the count will be high (particles below, say, 0 8 μ will contribute very little to the weight of a sample), and when the average particle size in a dust cloud is small, the mass concentration relative to the particle count is also small Again, a sample containing mainly sandstone dust particles will give a higher mass concentration value than one containing similar numbers of particles, with the same size distribution, taken from the air of a colliery

In practice, the difference between mass concentration and particle count values is less important than would appear at first sight. In most surveys, dusts of one type are measured, so that large variations in density are not likely to occur. Unless sampling is conducted very close to the source of the dust, the very large particles settle out by air elutriation before they reach the filter. Very small particles, which may be numerous, contribute little to the weight of the sample, and, so far as respiratory disease is concerned, it has been proved that these particles are of little importance.

The main objection to the use of mass concentration values has been eliminated by the work which Hamilton and Walton[600] have carried out on the design of elutriators for dust-sampling instruments. Hamilton and Walton recommend the use of a size-selecting elutriator which cuts out all particles of diameter greater than 7 μ. It is not feasible to obtain a sample from which all the particles above and none of the particles below the critical size are removed and the elutriator gives a graded retention curve—for example 50 per cent of the 5-μ particles are removed In the investigation of a dust hazard, this is not a disadvantage since the respiratory system also gives a graded retention curve

Hamilton and Walton have shown that the performance of a horizontal elutriator at a sampling rate, F, if the dust particles have a settlement velocity, f, is determined only by the floor area, A, of the elutriator and $A=F/f$ This floor area can be obtained by using either single or multiple horizontal plates.

The calculation of mass concentration figures from differential particle counts usually gives close agreement with the values obtained by the methods of mass concentration measurement Samples for mass concentration determination are easier to obtain, and far easier to evaluate, than are those required for particle counts· the latest methods of collection are simple and exact Moreover, a single sample can be taken over any length of time to give a value for the average dustiness, most methods for the determination of particle count are designed only to take snap samples, or at best, to sample the air over a period of a few minutes

Filtration methods

One of the earliest and simplest methods for the measurement of the mass concentration of dusts utilized a circle of filter paper through which air was drawn The volume was determined by passing the air through a meter and the paper was weighed before and after treatment the weight of dust in unit volume of air then being calculated The method was not too successful filter papers tend to become clogged by fine dust while oil or water droplets which are often present in industrial atmospheres very rapidly reduce filtration rate Moreover, cellulose is hygroscopic and the weight of the filter paper after sampling may have been increased appreciably Some workers ignited the paper and sample before weighing the dust, but ignition alters the composition of dusts

South African workers used pure cane sugar crystals as a filtering medium The crystals were packed into a glass tube and suction was applied through a narrower tube held in position by a rubber bung The filtered air was passed through a gas meter After the sample had been collected the crystals and the retained dust were washed out from the tube into a paper filter the sugar was dissolved in water and the dust sample was weighed usually after ignition Graham replaced cane sugar as a filtering medium by potassium nitrate

Salicylic acid crystal filters

The sugar tube has several disadvantages More satisfactory methods for the determination of the mass concentration of dusts were developed for the Medical Research Council s investigation[401] into conditions in the South Wales coalfields One of these makes use of a bed of loose crystals as a filter The crystals are those of an organic substance, usually salicylic acid which is readily soluble in an organic solvent and can easily be obtained pure The crystals are

connected to a suction device The filters are made at the sampling position as required The salicylic acid is divided into portions weighing 2 3 grams and each portion is wrapped in cellophane Before sampling the packet is opened and the cellophane is laid

made

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Salicylic acid crystal filters

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... cell assembly screws on to an ebonite funnel which can be connected to a suction device The filters are made at the sampling position as required The salicylic acid is divided into portions weighing 2–3 grams and each portion is wrapped in cellophane Before sampling, the packet is opened and the cellophane is laid

flat on the palm of the hand with the crystals in a heap. The inverted filter assembly is placed with its gauze surface on the crystals, then the whole is inverted. By tapping the cellophane an even filter bed is prepared without contamination. The stem of the funnel is then connected by a rubber hose to the compressed air ejector which is used as a source of suction, keeping the gauzes horizontal The cellophane is removed and the compressed air

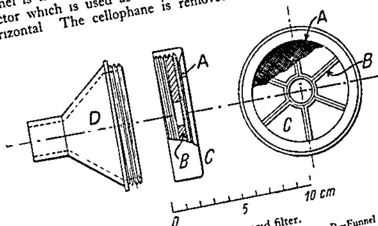


Fig 17 7. Salicylic acid filter.
A—Stainless steel gauzes, *B*—Ebonite grid, *C*—Cell holder, *D*—Funnel

supply to the injector is turned on; the filter is now stable and can be run in any position, although it is usual to take samples with the gauzes lying in a vertical plane. In the laboratory, the crystals and samples are transferred to a weighed centrifuge tube and the filter base is removed with hot solvent (alcohol if salicylic acid is used) After drying, the dust is weighed.

Loose crystal filters of this type are satisfactory only if a sufficiently powerful source of suction is provided; they are then reliable and have a high efficiency When compressed air is available at a pressure not less than 60 lb/in.², an ejector with a 1-mm. jet will provide sufficient pressure drop across the filter. If the ejector is fitted with a critical pressure orifice, the rate of flow is standardized so that no flow meter is required These filters are capable of handling large volumes of air and their efficiency increases with the rate of sampling.

The naphthalene filter

The extensive study of the atmospheres of South Wales coal-mines, which was commenced in 1937 by the Medical Research Council,

required the measurement of the mass concentration of dust at a large number of points in many different collieries The hundreds of samples necessary could not be obtained conveniently by a method which needed compressed air lines at every sampling point The alternative method of sampling which was developed is one of the simplest and most convenient procedures available, yet it enables [illegible]

platinum or aluminium dish The naphthalene is removed by heating the dish to a temperature slightly below 80°C when it sublimes away leaving an uncontaminated dust sample A second weighing enables the mass of the dust to be determined Weighings are carried out on a microbalance enabling samples as small as 20–30 micrograms to be accurately estimated

Naphthalene filter samples may be taken by means of a hand pump of known stroke volume (ordinarily 100 ml) and this method is usually satisfactory in collieries, where dust concentration is high The volume sampled must contain not much less than 30 micrograms of dust An electrically driven sampling pump has been designed which, sampling at a rate of 2 000 ml /min can be left running without attention

[illegible]

under reduced pressure

The design of the filter holder is shown in Fig 17 8 The outer case is in the form of a double cone and the filter can be plugged directly into a socket in the sampling pump

The Hexhlet sampler

Wright[602] described a sampling instrument, designed for use in coal-mines, which collects the sample in a Soxhlet thimble through which air is drawn by a compressed air ejector In front of the thimble there is an air elutriator designed to prevent large particles from reaching the filter The rate of flow is controlled by a critical flow orifice attached to the air ejector As a filter for dust collection,

Soxhlet thimbles have the disadvantage that about 100 mg of the dust becomes permanently trapped in the pores of the thimble

Wright[803] also described a thermal precipitator which would collect dust samples large enough for gravimetric estimation It has an aluminium collecting plate spaced about 0·015 in. from a steel heating plate.

Photoelectric methods

The methods of dust collection which have been described are designed to give a picture either of the mass concentration of the dust over a sampling period of minutes or hours, or a figure for particle count during a period of seconds or minutes The field sample must be evaluated in the laboratory later, and this may take some hours

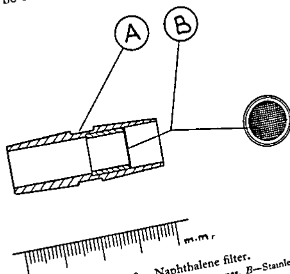


Fig 17.8 Naphthalene filter.
A—Stainless steel tube consisting of two cones, *B*—Stainless steel gauze

To facilitate dust control, it would be of great value if counts and mass concentration figures could be obtained immediately. Average mass concentration figures over a shift are easy to obtain, but average figures for particle counts require the evaluation of a large number of samples, a tedious and time-consuming procedure.

A considerable amount of effort has gone into the design of instruments which measure photoelectrically the absorption or reflection of light by dust particles, and can give an instantaneous value which is

related to the dustiness of the atmosphere The earliest instrument of this type interposed a sample of the dust laden air between a light source and a photoelectric cell Absorption of light by the dust particles produces a decrease in the e m f induced in the cell The new e m f can be measured by a sensitive milliameter and the decrease in the current is proportional to the dust concentration

A more satisfactory type of instrument utilizes the Tyndall effect [illegible]

readings cannot be translated into particle counts or into mass concentration values Provided that the type of dust and size grading is reasonably constant the Tyndallometer values do vary in a similar manner to the counts and mass concentration figures however

The dust concentration in many industrial atmospheres is too small for the application of the direct photoelectric methods described It is possible to multiply the response of the photocell to almost any degree but if the amplification is too great the 'background' of the instrument is so high that the results become at least inaccurate and often meaningless

Holt and Chalk[404] described a method of collecting samples by a filter similar to the naphthalene filter described earlier then re suspending the sample in an organic liquid and measuring the con centration of the dust in the suspension by a Tyndallometric method [illegible]

particle count were satisfactory

The collection of massive dust samples

Large samples of dust are usually required only when fundamental research is to be carried out into the nature and properties of a dust cloud For this purpose it is essential to obtain a sample which is truly representative of the air-borne dust No segregation is permis sible, either with respect to particle size or to composition The apparatus which is suitable for this purpose varies with the concentration of the dust cloud to be handled With many dusts filter paper clogs rapidly, but filter paper is sometimes used when the dust concentration is low Beryllia, for example, is seldom present in industrial atmospheres in concentrations larger than a fraction of a milligram per cubic metre The air is drawn at high velocity through

incidentally to the mining or quarrying of other minerals [illegible]

(*b*) [illegible]

operations.

2 Any occupation involving the breaking, crushing or grinding of flint or the working or handling of broken, crushed or ground flint or materials containing such flint, or substantial exposure to the dust arising from any of such operations

3 Any occupation [illegible]

(*a*) the freeing of steel castings from adherent siliceous substance,
(*b*) the freeing of metal castings from adherent siliceous substance:

(i) by blasting with an abrasive propelled by compressed air, by steam or by a wheel; or
(ii) by the use of power-driven tools.

5 Any occupation in or incidental to the manufacture of china or earthenware (including sanitary earthenware, electrical earthenware and earthenware tiles), and any occupation involving substantial exposure to the dust arising therefrom

6. Any occupation involving the grinding of mineral graphite, or substantial exposure to the dust arising from such grinding.

7. Any occupation involving the dressing of granite or any igneous rock by masons or the crushing of such materials, or substantial exposure to the dust arising from such operations.

8 Any occupation involving the use, or preparation for use, of a grindstone, or substantial exposure to the dust arising therefrom.

9 Any occupation involving.

(*a*) the working or handling of asbestos or any admixture of asbestos;
(*b*) the manufacture or repair of asbestos textiles or other articles [illegible]

(*c*) [illegible]

(*d*) substantial exposure to the dust arising from any of the foregoing operations.

10 Any occupation involving:

(*a*) [illegible] objects of the [illegible]

(*b*) [illegible] tin mine of [illegible] n incidental thereto,

(*c*) the trimming of coal in any ship, barge or lighter, or in any dock or harbour or at any wharf or quay;
(*d*) the sawing, splitting or dressing of slate, or any operation incidental thereto.

11 Any occupation in or incidental to the manufacture of carbon electrodes by an industrial undertaking for use in the electrolytic extraction of [illegible]

The National Insurance (Industrial Injuries) Act provides compensation for persons who contracted pneumoconiosis and were working in one or more of the specified occupations on or after July 5, 1948 Most persons who had contracted the disease before that date were eligible for compensation under the Workmen's Compensation Acts Under these two Acts certain persons were excluded from benefit To meet these cases the Pneumoconiosis and Byssinosis Benefit Act, 1951, provided benefit to be paid from the Industrial Injuries Fund where a workman was totally disabled or had died from pneumoconiosis but was unable to claim under Workmen's Compensation Acts because he had left the specified occupation before these Acts were extended to cover it, or because no diagnosis of the disease was made within the time specified by the Acts The details were given in the Pneumoconiosis and Byssinosis Benefits Scheme, 1952, which is administered by an independent Benefit Board appointed by the Minister of Pensions and National Insurance

The Pneumoconiosis and Byssinosis Benefit Amendment Scheme, 1954, extended the benefits allowed by the Pneumoconiosis and Byssinosis Scheme, 1952, to persons who were not totally disabled but were partially disabled by pneumoconiosis An Act has recently been passed (National Insurance Act, 1954) which increases the rates of benefit allowable under the Industrial Acts, and this applies, of course, to persons who are awarded benefit for death or disablement from pneumoconiosis

A person who has not worked in one of the specified occupations may be entitled nevertheless to benefit if he can satisfy a Pneumoconiosis Medical Board that he is suffering from pneumoconiosis contracted whilst working in some other occupation

Normally, claims for compensation for pneumoconiosis are first judged by the examination of X-ray films of the chest of the worker The examination is made by a medical man who is a member of a Pneumoconiosis Medical Panel Appeals against the decision of a member of the Panel are heard by a Pneumoconiosis Medical Board, consisting of two members of the Panel A similar Board also assesses the degree of disablement when a claim is allowed The assessment is based on loss of faculty due to the disease, the basic rate of compensation depends only on this and does not take into account such factors as the loss of earning power or the nature of

employment. These factors may justify certain supplementation to the basic rate, however. For 100 per cent disablement due to silicosis the basic disablement pension is 55*s*. weekly.

Employer's liability

Under various Acts of Parliament, an employer is required to take precautions intended to minimize the risk involved in handling materials which can cause pneumoconiosis. Failure to comply with these requirements may render the employer liable to pay compensation if his negligence has contributed to a pneumoconiosis hazard to which an employee is exposed. *Examples of provisions in the Factory* and Workshops Acts, which may be relevant to an industry handling materials constituting a hazard, are:

Factories Act, 1937. Section 1. The floor of every workroom shall be cleaned at least once in every week by washing or, if it is effective and suitable, by sweeping or other method

Section 47. In every factory in which, in connection with any process carried on, there is given off any dust or fume or other impurity of such a character and to such extent as to be likely to be injurious or offensive to the persons employed, or any substantial quantity of dust of any kind, all practicable measures shall be taken to protect the persons employed against inhalation of the dust or fume or other impurity and to prevent its accumulating in any workroom, and in particular, where the nature of the process makes it practicable, exhaust appliances shall be provided and maintained, as near as possible to the point of origin of the dust or fume or other impurity, so as to prevent it entering the air of any workroom

Special regulations which apply to iron and steel foundries (Iron and Steel Foundries Regulations, 1953) include:

All *knock-out operations* (removal of castings from moulds) shall be carried out

(*a*) [illegible]

(*b*) in an area of the foundry in which, so far as *reasonably practicable*, effective and suitable local exhaust ventilation is provided, *or where compliance with the requirement is not reasonably practicable, a high* standard of general ventilation is provided

All *dressing or fettling operations* (removal of adherent sand from the castings) shall be carried out.

(*a*) in a separate room or in a separate *part of the foundry suitably* partitioned off, or

(*b*) in an area of the foundry set apart for the purpose

and shall, so far as reasonably practicable, be carried out with effective and suitable local exhaust ventilation or other equally effective means of suppressing dust, operating as near as possible to the point of origin of the dust.

Protective equipment The occupier shall provide and maintain *approved respirators* for workers carrying out any operation creating a heavy dust concentration which cannot be dispelled quickly and effectively by the existing ventilation arrangements

Each *respirator* provided for the purposes of this Regulation shall carry a distinguishing mark indicating the person by whom it is intended to be used and no person shall wear or be required to wear a *respirator* not carrying his mark or a *respirator* which has been worn by another person and has not since been thoroughly disinfected

Every employed person shall make full and proper use of the equipment provided for his protection and shall without delay report to the occupier, manager or other appropriate person any defect in, or loss of the same

The only *respirators* which are approved and can be used at present are the Mark IV and the Micro-filter, and definite means of identification, cleaning and disinfecting should be established

The regulations make it clear that the employer is not only required to provide protective equipment but he must also make certain that the worker uses it Should a claim of negligence arise the Court is likely to consider the effort made by the employer to acquaint the workman with the risk to which he is exposed and to impress him with the necessity for taking precautions The Court is likely, also, to take into account the diligence with which safety requirements have been enforced It is advisable for a firm to keep records of the issue and maintenance of respirators and also of warnings and disciplinary action which may have to be made when employees fail to take the prescribed precautions

The following regulations (Blasting (Castings and other Articles) Special Regulations, 1949) refer specifically to the blasting and cleaning of castings

except blasting and work immediately incidental thereto and the cleaning and repairing of the enclosure and of plant and appliances situated therein Every door of a blasting enclosure shall be kept closed while blasting is being done therein

Maintenance of blasting enclosure Blasting enclosures shall be constantly maintained in good condition and all practicable measures shall be taken to prevent dust escaping from such enclosures and from any apparatus connected therewith, into the air of any room

Provision of separating apparatus There shall be provided and maintained in connection with every blasting enclosure efficient apparatus for separating so far as practicable abrasive which has been used in blasting apparatus and which is to be used again as an abrasive from dust or particles of other material arising from blasting and no such abrasive shall again be introduced into blasting apparatus until it has been so separated

Provided that this Regulation shall not apply (except in the case of blasting

chambers) to blasting enclosure-

...such persons are
...attending to such bag or other filtering or
setting device shall be completely separated f...
room in an enclo...

Operation
purposes of
ever the bl.
taking place ... a blasting chamber shall be in opera-
tion when any person is inside the chamber for the purpose of clea...
or repair work

...ation or test shall be immediately
r...ed by the person carrying out the inspection, examination or test to
the occupier, manager or other appropriate person and without prejudice to
the foregoing requirements of these Regulations shall be remedied without
avoidable delay

The Foundries (Parting Materials) S...

Dust or other matter deposited from a fettling or blasting process shall
not be used as a parting material or as a constituent in a parting material.

Regulations relevant ...
were given in the Gri...
Regulations, 1925. Th...

Metals (Miscellaneous Industries) (Amendment) Special Regulations, 1950 The Regulations of 1925 state

No *racing*, dry *grinding* or *glazing* ordinarily causing the evolution of dust into the air of the room in such a manner as to be inhaled by any person employed shall be performed without the use of adequate appliances for the interception of the dust as near as possible to the point of origin thereof and for its removal and disposal so that it shall not enter any occupied room, and for the purpose of this Regulation the appliances shall not be deemed adequate unless they either include

(*a*) a hood or other appliance, so constructed, arranged and placed as substantially to intercept the dust thrown off and

(*b*) a duct of adequate size, air tight and so arranged as to be capable of carrying away the dust, which duct shall be kept free from obstruction and shall be provided with proper means of access for inspection and cleaning, and, where practicable, with a connection at the end remote from the fan to enable H M Inspector of Factories to attach thereto any instrument necessary for ascertaining the pressure of air in the said duct, and

(*c*) a fan or other efficient means of producing a draught sufficient to extract the dust,

or are such as, in the case of the particular factory or part thereof or of the particular manufacture, process or operation in or for which they are used, shall be proved to be at least as effectual for such interception removal and disposal as such hood, duct and fan would be

In every room in which wet *grinding* upon a *grindstone* is carried on there shall be provided and maintained whilst work is in progress either

(*a*) adequate exhaust and inlet ventilation or

(*b*) a supply of clean water conveyed by pipes and deposited upon the surface of the *grindstone*, and suitable arrangements to ensure the drainage of the waste water from the *grindstone* trough

For the purposes of this Regulation the ventilation shall not be deemed to be adequate unless (i) it ensures that the air of the room is renewed not less than 12 times per hour, (ii) it is arranged in such a manner as to secure a continuous movement of the air in a direction from the grinder towards the *grindstone*, and (iii) the fresh air inlets are so arranged and are of such dimensions that no worker is exposed to a direct draught from them

Not more than one person shall at any time be allowed to perform the actual process of *grinding* or *glazing* upon any *grindstone*, *abrasive wheel* or *glazing* appliance

Provided that this Regulation shall not prohibit the employment of persons to assist in the manipulation of heavy or bulky articles at any such *grindstone*, *abrasive wheel* or *glazing* appliance

Glazing or other processes, except processes incidental to wet *grinding* upon a *grindstone*, shall not be carried on in any room in which wet *grinding* upon a *grindstone* is done

Wet *grinding* upon a *grindstone* shall not be done in any room

(*a*) in which the height of the room, measured from any part of the floor to the lowest part of the top is less than 10 feet, nor

(*b*) in which the total window area is less than one-sixth of the floor area nor

(c) unless all the windows are properly glazed and the glass or other material of such windows maintained whole and kept clean

Hacking or *rodding* shall not be done unless during the
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condition so as to permit of such
sweeping or cleaning

Provided that this Regulation shall not apply to·

(i) *cleaning of castings* done upon the foundry floor at or near the place where the metal for the said castings is poured; or
(ii) any room wherein the only castings dealt with are those which have been freed from sand elsewhere; or
(iii) *rumbling* done in any room in which no other work is ordinarily performed if no person is wholly or mainly employed in the process

A register containing the dates and particulars of all sweeping or cleaning done in pursuance of these Regulations and the name and the address of the person performing the
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(a) the *rumbling* appliance is provided with efficient exhaust draught arranged and maintained so that any dust evolved is prevented from entering any occupied room; or
(b) such other arrangements are made as shall be proved to be at least as effective in preventing the dust from entering any occupied room.

Provided that this Regulation shall not apply to *rumbling* done in any room in which no other work is ordinarily performed if no person is wholly or mainly employed in the process.

* * * * *

(a) All ventilating plant used for the purpose of extracting or suppressing dust shall at least once in every six months be examined and tested by a competent person, and any defect disclosed by such examination and test shall be rectified as soon as practicable

(b) A register containing particulars of such examination and test shall be kept in a form approved by the Chief Inspector of Factories and shall be available for inspection by any workman employed in any room in respect of which the ventilating plant is provided

Every person who is employed or engaged in any work to which these Regulations apply shall make full and proper use of all appliances, facilities or accommodation provided for any of the purposes of these Regulations and shall report forthwith to the owner, occupier, manager or other responsible person any defect in the same

The ventilation of workshops where processes related to the pottery industry are carried out is dealt with in the Pottery (Health and Welfare) Special Regulations, 1950 The following are extracts from these Regulations

The following processes shall not be carried on without the use of an efficient draught

(i) the manipulation of calcined flint at the mouth of the calcining kiln, unless the material has been made and remains so wet that no dust is given off,

(ii) the sieving of material drawn from the calcining kiln after the calcining of flint, unless the material has been made and remains so wet that no dust is given off,

(iii) the crushing or grinding of flint or quartz, unless the material has been made and remains so wet, or the process is carried on in a machine or plant which is so enclosed, as effectually to prevent the escape of dust into the air of any place where any person works,

(iv) the dry grinding of any material other than flint or quartz for a pottery body, unless the process is carried on in a machine or plant which is so enclosed as effectually to prevent the escape of dust into the air of any place where any person works,

(v) the sifting of clay dust for making tiles or other pottery articles by pressure, unless the material is so damp that no dust is given off

(vi) the loading or unloading of calcined flint or of quartz or clay dust into or from any container or machine, unless the material is so damp that no dust is given off,

(vii) fettling other than damp fettling,

(viii) damp fettling unless suitable arrangements are made for collecting scraps from the fettling and, except in the case of sanitary fireclay ware, for preventing them from falling onto the floor,

(ix) the pressing of tiles or (unless the material is so damp that no dust is given off) of other articles from clay dust, and in any such case the exhaust draught shall be applied to the dies of each press and to the stock-boxes containing the dust

(x) the brushing of earthenware biscuit including earthenware tile biscuit and sanitary earthenware biscuit, unless the process is carried on in a room provided with a system of general ventilation effected with the aid of mechanical means, being a system which is

certified by the Inspector for the District as being adequate in the circumstances of the case if properly maintained and which is in fact properly maintained,

(xi) the placing of china for the biscuit fire if alumina or other powdered material is used;
(xii) the emptying of china biscuit flat-ware from saggars after firing in alumina or other powdered material,
(xiii) flat-knocking,
(xiv) the scouring of china biscuit by brushing or rumbling, if alumina or other powdered substance has been used as a placing material;
(xv) [illegible]
(xvi)
(xvii)

(b) while the article is so damp that no dust is given off;

(xviii) the preparation or weighing out of flow material;
(xix) the lawning of dry colours, except where not more than one ounce at a time is lawned for use in painting;
(xx) glaze spraying or glaze blowing;
(xxi) colour blowing or the wiping off of colour after that process;
(xxii) ground laying or colour dusting, or the wiping off of colour after either of those processes;
(xxiii) lithographic transfer making with dry colours;
(xxiv) the polishing of ware;
(xxv) [illegible] on a dry sandstone wheel;
(xxvi)
(xxvii)

Every process for which an exhaust draught is required by this Regulation shall be carried on inside a suitable hood: provided that where this is impracticable it shall be sufficient if the work is done within the effective range of an exhaust opening.

All screens and sieves and all chutes, conveyors, elevators and mixers used for manipulating materials containing flint or quartz so dry as to produce dust shall be enclosed and be provided with an efficient exhaust draught

In connection with ware-cleaning, suitable arrangements shall be made for any glaze dust or glaze scraps not removed by exhaust draught to fall into water

[illegible] glaze spraying or glaze blowing or colour blowing is

[illegible]

of ventilating plant used solely in connection with any of [illegible] processes:

(i) the brushing of eathenware biscuit;
(ii) ware-cleaning;
(iii) ground laying or colour dusting;
(iv) the polishing of ware;

(v) the sorting of glost ware with a power driven tool
(vi) the grinding of tiles on a power driven wheel

Air discharged from exhaust ventilating plant used in connection with any of the processes specified above (i) to (xxviii) shall whether or not it has passed through dust collecting apparatus be discharged directly into the open air where it is not liable to be drawn into the air of any work room

All ventilating plant and dust collecting apparatus required by this Regulation shall be properly maintained and shall at least once in every period of fourteen months be thoroughly examined and tested by a competent person and a report of the result of every such examination and test signed by the person making the examination and test and including particulars as to the state of the plant and any defects found shall forthwith be entered in a register which shall be kept at the factory in a form approved by the Chief Inspector

The Pottery (Health) Special Regulations 1947 specifically prohibited the use of certain materials in a dry form

Ground or powdered flint or quartz with or without the addition of other materials shall not be used in any factory to which these Regulations apply or any of the following purposes

(a) the placing of ware for the biscuit fire
(b) the polishing of ware
(c) as an ingredient in a wash for saggars trucks bats cranks or other articles used in supporting ware during firing
(d) as dusting or supporting powder in potters shops

(1) There shall not be brought into or used in any factory to which these Regulations apply any ground or powdered flint or quartz other than ground or powdered flint or quartz which forms part of a slop or paste

(2) The prohibitions in paragraph (1) hereof shall not apply to a separate room or building in a factory being a room or building

(a) which is used for any of the following purposes that is to say the manufacture of ground or powdered flint or quartz or the making of frits or glazes or the making of colours or coloured slips for the decoration of pottery and
(b) which is not used for any other process in or incidental to the manufacture or decoration of pottery

(3) Notwithstanding the prohibitions in paragraph (1) hereof ground or powdered flint or quartz may be brought into kept and moved in a factory in bags or other containers so made or so closed or sealed as to prevent the escape of dust therefrom and after being so brought in and before or while being mixed with other materials to form the body of the ware may be subjected to any process movement or treatment which is effected by mechanical means and carried on in an enclosure in which no person is employed and which is so constructed and ventilated as to prevent the escape of the dust into any place where persons are employed

Regulations which relate to industries in which asbestos is used are described in the Asbestos Industry Regulations 1931

Duties of Occupiers

1 An exhaust draught effected by mechanical means which prevents the escape of *asbestos dust* into the air of any room in which persons work, shall be provided and maintained for:

(*a*) manufacturing and conveying machinery, namely:

(i) *preparing*, grinding or dry mixing machines;
(ii) carding, card waste-end, ring spinning machines, and looms,
(iii) machines or other plant fed with *asbestos*;
(iv) machines used for the sawing, grinding, turning, abrading or polishing, in the dry state, of articles composed wholly or partly of *asbestos*;

(*b*) cleaning and grinding of the cylinders or other part of a carding machine,
(*c*) chambers, hoppers or other structures into which loose *asbestos* is delivered or passes,
(*d*) work benches for *asbestos* waste sorting or for other manipulation of *asbestos* by hand,
(*e*) work places at which the filling or emptying of sacks, skips or other portable containers, weighing, or other process incidental thereto which *is effected by hand, is carried on;*
(*f*) sack-cleaning machines

Provided that this Regulation shall not apply (i) to a machine or other plant which does not give rise to *asbestos* dust, or is so enclosed as to prevent escape of *asbestos* dust into the air of any room in which persons work, or (ii) where the *asbestos* is so wet or so treated with grease or other material as to prevent the evolution of dust, or (iii) to the making or repairing of insulating mattresses, or (iv) to mixing or blending by hand of *asbestos*

2 —(*a*) Mixing or blending by hand of *asbestos* shall not be carried on except with an exhaust draught effected by mechanical means so designed *and maintained as to ensure as far as practicable* the suppression of dust during the process

(*b*) In premises which are constructed or reconstructed after the date of [illegible] shall not be done except

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work is done

(ii) In every room in which the making or repairing of insulating mattresses is carried on

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[illegible] benches shall be kept damped so as effectually to prevent

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4.—(a) Storage chambers or bins for loose *asbestos* shall in the case of premises constructed or reconstructed after the date of these Regulations be effectually separated from any workroom and in the case of other premises be effectually separated from any workroom in which the *asbestos* is not required for the purposes of any process carried on in the room

(b) chambers or apparatus for dust settling and filtering shall not be allowed in any workroom

(c) arrangements shall be made to prevent *asbestos* dust discharged from exhaust apparatus being drawn into the air of any workroom

5 All machinery used in *preparing* grinding of *asbestos* carding card roller cleaning and grinding and sack cleaning and all card waste end machines lattices elevators chutes and conveyors shall be so constructed and maintained that dust or debris containing *asbestos* cannot escape from any part thereof other than dust removed by an exhaust draught provided in accordance with Regulation 1

6.—(a) Cleaning by hand of the cylinders (including the doffer cylinders) of a carding machine shall not be done whilst any person other than those performing or assisting at the cleaning is present

(b) On and after the 1st September 1932 such cleaning as aforesaid shall not be done by means of hand strickles or other hand tools

7.—(1) In every room in which any of the requirements of these Regulations apply

(a) the floors work benches and plant shall be kept in a cleanly state and free from *asbestos* debris and suitable arrangements shall be made for the storage of *asbestos* not immediately required for use

(b) the floors shall be kept free from any materials plant or other articles not immediately required for the work carried on in the room which would obstruct the proper cleaning of the floor and

(2) every room as aforesaid shall be adequately lighted

8.—(a) A sack which has contained *asbestos* shall not be cleaned by hand beating but by a machine complying with Regulations 1 and 5

(b) All sacks used as containers for the transport of *asbestos* within the factory shall be constructed of impermeable material and shall be kept in good repair

9.—(a) All ventilat[illegible]
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[illegible] dust settling or filtering chambers or apparatus

(c) in cleaning the cylinders including the doffer cylinders or other part of a carding machine by means of hand strickles

(d) in filling beating or levelling in the manufacture or repair of insulating mattresses

11 There shall be provided and maintained for the use of all persons employed in the cleaning of dust settling and filtering chambers tunnels and ducts suitable overalls and head coverings

12 A young person shall not be employed in or in connection with the manufacture of insulating mattresses, in mixing or blending of *asbestos* by [illegible] in chambers or apparatus for dust settling or filtering, [illegible] stripping or grinding the cylinders [illegible] chine [illegible] young person so [illegible]

Duties of Persons Employed

13. No person employed shall wilfully or negligently disregard any directions given him for the purpose of securing the observance of these Regulations or otherwise for the prevention of unnecessary dust.

14 Every person employed shall make full and proper use of the appliances provided for any of the purposes of these Regulations

15. No person shall misuse or wrongfully interfere in any way with any appliance provided in pursuance of these Regulations

16. Every person employed at work specified in Regulation 10 shall wear and make proper use of the *breathing apparatus* provided in pursuance of that Regulation.

17 Every person employed at the work specified in Regulation 11 shall wear the overall and head-covering provided in pursuance of that Regulation

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